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Status of Prostate Specific Antigen and Alpha Fetoprotein in Nigerian E-Waste Workers: A Cancer Risk Predictive Study

Igharo OG[1,2*], **Anetor JI**[2], **Osibanjo OO**[3], **Osadolor HB**[1], **Aiyanyor DO**[1] **and David OM**[1]

[1]*Department of Medical Laboratory Sciences, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City, Nigeria*

[2]*Toxicology and Micronutrient Metabolism Unit, Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria*

[3]*Basel Convention Coordinating Centre for Training & Technology Transfer for the African Region & Department of Chemistry University of Ibadan, Oyo State, Nigeria*

[*]**Corresponding author:** Igharo OG, Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria, Tel: +2348038664896; E-mail: godwingreatman@yahoo.com

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Abstract

Nigeria is reported as the largest electronic waste (e-waste) dump yard in Africa; and to date, Nigeria's e-waste management practices remain completely primitive. It was recently documented that the majority (88.8%) of Nigerian e-waste workers (with exposure burden of ≥ 6 hours per day; ≥ 6 days per week) worked without personal protective devices inspite of the volume of toxic substances, some of which are known carcinogens, documented to be found in e-waste. The present study aimed to evaluate the status of Prostate Specific Antigen (PSA) and Alpha Fetoprotein (AFP) as cancer risk biomarkers in Nigerians occupationally exposed to waste electrical and electronic equipment (also known as e-waste) in Benin City, Nigeria. Serum levels of PSA and AFP were determined in Nigerian e-waste workers (n=63) and in age-matched non-exposed participants (n=41), using Enzyme linked Immunosorbent Assay. It was observed that PSA and AFP levels in e-waste workers (12.62 ± 6.0 ng/ml; 3.56 ± 0.34 ng/ml) were significantly elevated compared with the non-exposed group (2.14 ± 0.38 ng/ml; 2.14 ± 0.80 ng/ml), (P=0.000 and P<0.045) respectively. In addition, 26% of e-waste workers compared with 11% of non-exposed participants registered higher than the reference range of PSA (0-4.0 ng/ml) used for healthy subjects. This study concludes that the significantly elevated cancer risk biomarkers (PSA and AFP) observed in the studied population of Nigerian e-waste workers may be associated with occupational exposure to known carcinogens in e-waste.

Keywords: Prostate specific antigen; Alpha fetoprotein; Cancer; E-waste; Nigerian

Introduction

Electronic waste, e-waste, e-scrap, or waste electrical and electronic equipment (WEEE) describes discarded electrical or electronic devices. The term may broadly be defined as discarded computers, office electronic equipment, entertainment device electronics, mobile phones, television sets and refrigerators [1]. WEEE have been reported to contain numerous carcinogenic chemicals, which include mercury, lead oxide, cadmium, and polyvinyl chloride [1,2].

In Nigeria and most developing countries, e-waste management practices remain primitive and take place mainly in the informal sector. This informal processing may result in serious health and pollution problems, particularly as the developing countries are more likely to reuse and repair electronics than developed countries. It has been reported that e-waste disposal become especially problematic when humans and the environment come in contact with hazardous chemicals during the process of dismantling electronic products [2].

Humans can become exposed to heavy metals in dust through several routes, including ingestion, inhalation, and dermal absorption [3,4]. In dusty environments, it has been estimated that adults could ingest up to 100 mg dust/day [4,5]. Exposure to high levels of heavy metals can result in acute and chronic toxicities in organs and systems of the body. There is a serious association between heavy metal and chemical toxicants, and high cancer risks [3].

Prostate cancer is a leading cause of cancer-related death of men globally. Prostate cancer is the most common cancer in Nigerian males; having overtaken liver cancer. Liver cancer is the most common cause of cancer death in Nigeria; and the most common liver malignancy in Nigeria is hepatocellular carcinoma [6].

This study aimed at evaluating the status of prostate specific antigen and alpha fetoprotein as cancer risk biomarkers in Nigerians occupationally exposed to e-waste in Benin City, Nigeria.

Participants and Methods

Study design

This research was designed as a comparative study between occupationally exposed and unexposed groups.

Study area

This study was carried out in the Metropolitan City of Benin, Edo State, South-South Nigeria. Benin City is the current capital of Edo State with an estimated average population of 1,147,188 in the 2006 General Census.

Study Population

Exposed group

Male Waste Electric and Electronic Equipment (WEEE) Workers (n =63, Mean age of 31 years) working and living in Benin City, formed the exposed group. The states of origin of the exposed subjects comprised of Edo, n=32 (50.8%); Imo, n=15 (23.8%); Delta, n=7 (11.1%); Anambra, n=3 (4.8%); Ekiti, n=2; (3.2%); Enugu, n=2 (3.2%) and Abia, n=2 (3.2%). Only subjects with a minimum of 5 years of occupational exposure to toxic substances in WEEE were enrolled into the study.

Unexposed group

Age-matched apparently healthy male participants, with minimal or no occupational exposure to toxic substances in WEEE, who were recruited from the Ugbowo Campus Community of the University of Benin formed the non-exposed group in this study.

Inclusion criteria

Exposed subjects comprised of electronic technicians carrying out informal (primitive) e-waste recycling, processing, repair and dismantling repair of electronic and electrical equipment. Subjects who were occupationally exposed to e-waste for a period of five years and above at the time of sample collection were considered suitable for the study.

Five years duration of exposure is based on E-waste Risk Assessment Report of Adaramodu, et al. [7].

Control subjects were apparently healthy male individuals with minimal or no occupational exposure and with no hobby involving e-waste exposure. The non-exposed participants had no previous demographic and medical history of incidence of cancer.

Exclusion criteria

E-waste workers who are not exposed to e-waste for a period up to five years at the time of sample collection would not be considered suitable for the study. Subject with history of any form of cancer, tobacco smoking and alcoholism would be excluded from the study. Tobacco smoking and alcohol consumption shall also serve as basis of exclusion for recruiting the apparently healthy control subjects.

Ethical approval

The protocol for this study was approved by the Health Research Ethics Committee of University of Ibadan/University College Hospital, Ibadan, Nigeria (UI/UCH EC Registration Number: NHREC/05/01/2008a).

Informed consent

Subjects for this study shall be adults who would have been adequately briefed on the research protocol and informed consent shall be obtained prior to sample collection. The informed consent form to be used for this study shall be explicitly explained to the participants in English and in their local dialect.

Sample collection

Approximately ten millilitres of venous blood was collected from test subjects (e-waste workers) and control subjects using standard phlebotomy techniques. Blood samples obtained were dispensed (five millilitres) into EDTA anticoagulant specimen bottles until time of analysis. Another five millilitres was dispensed into anticoagulant-free bottles to obtain serum. Information about exposure burden was obtained by means of questionnaires provided to the participants of the study.

Laboratory analysis

Concentrations of prostate specific antigen and alpha fetoprotein in the samples were estimated by enzyme linked immunosorbent assay (ELISA), as respectively described by Vessella et al. [8] and Stowell et al. [9].

All biochemical assays were carried out in the Clinical Chemistry Laboratory of the Department of Medical Laboratory Science, University of Benin, Benin City.

Statistical analysis

Statistical analyses including descriptive statistics were carried out using the statistical package for social scientists (SPSS) version 16.0. All values were expressed as Mean ± Standard Error of the Mean. The independent student's t-test was used to determine significant differences between exposed and unexposed groups and p value <0.05 was accepted (Table 1).

Results

Observation	Exposed Participant(n=63) Median Age=31 Years	Unexposed Participants (n=41) Median Age=29 Years
Duration of Exposure to E-waste Chemicals	≥ 5.0 Years	No Occupational Exposure
Frequency of Exposure to E-waste Chemicals	≥ 6 days /week	Nil
Routes of Exposure: Direct Indirect	Hands, eyes, nasal cavity, oral cavity, dermal absorption Environmental (high)	Nil Minimal
% Using Personal Protective Devices(PPDs) while working	Yes { (n=7) 11.1%} No { (n=56) 88.9 %}	Not Applicable
Specified PPDs used	Apron (cotton)	Not Applicable

Table 1: Occupational exposure burden of electronic waste workers compared with un-exposed participants in Benin City, South-South Nigeria.

Frequency of exposure to e-waste of greater than or equal to 6 days per week, and exposure routes such as hands, eyes, nasal cavity, and oral cavity, and through dermal absorption among the e-waste workers studied was observed. In addition, majority (88.9%) of the e-waste workers did not use personal protective devices (PPDs) such as apron, hand gloves and facemasks while working.

Figures 1 and 2 indicate levels of cancer risk biomarkers for prostate and liver in e- waste exposed workers and unexposed participants in Benin City, South-South Nigeria. PSA and AFP levels in e-waste workers (12.62 ± 6.0 ng/ml ; 3.56 ± 0.34 ng/ml) were significantly elevated compared with the non-exposed group (2.14 ± 0.38 ng/ml; 2.14 ± 0.80 ng/ml), (P=0.000 and P<0.045) respectively. Values are in mean ± standard errors of the mean (Table 2).

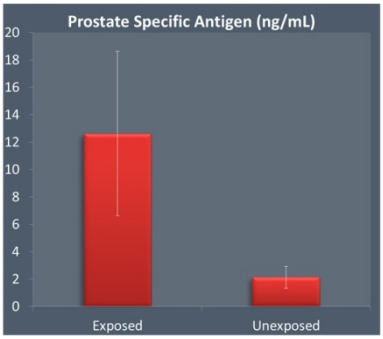

Figure 1: Comparison of blood levels of cancer risk biomarker (prostate-specific antigen) in e-waste exposed workers and unexposed participants in Benin City, Nigeria.

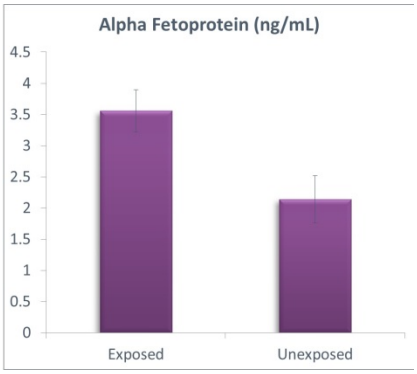

Figure 2: Comparison of blood levels of cancer risk biomarker (alpa fetoprotein) in e-waste exposed workers and unexposed participants in Benin City, Nigeria.

Participants (N=86)	>4.0 ng/ml (*R.R.H.P)	>4.0 ng/ml (*R.R.H.P)
E-waste Exposed Group (n=50)	n=13 (26.0%)	n=37 (74.0%)
Non-exposed Group (n=36)	n=4 (11.1%)	n=32 (88.9%)

Table 2: Prevalence of elevated PSA Levels in e-waste exposed and non-exposed groups in Benin City, Nigeria. ***R.R.H.P: reference range used for PSA values in healthy population (<4.0 ng/ml).**

Discussion

Prostate cancer is a leading cause of cancer-related death of men globally. Prostate Cancer is the most common cancer in Nigerian males; having overtaken liver cancer. Liver cancer is the most common cause of cancer death in Nigeria and most common liver malignancy in Nigeria is hepatocellular carcinoma. Liver disease is listed as a risk factor for cancer [6].

In this study, the status of PSA and AFP as cancer risk biomarkers were investigated in Nigerian e-waste workers. It was observed that mean PSA level in the e-waste exposed group (12.62 ± 6.00 ng/ml) was significantly higher compared with non-exposed participants (2.14 ± 0.80 ng/ml), p=0.000. In addition, 26% of e-waste workers compared with 11% of non-exposed participants registered higher than the reference range of PSA (0-4.0 ng/ml) used for healthy subjects.

Metal-induced oxidative damage is a known mechanism of carcinogenesis [10]. Metals may affect the male reproductive system directly, when they target specific reproductive organs, or indirectly, when they act on the neuroendocrine system. Prostate cancer is dependent on male sex steroid hormone for development, growth and survival. Cadmim, which is present in WEEE is a known endocrine disruptor. PSA is produced in the epithelial cells of the prostate, and can be demonstrated in biopsy samples or other histological specimens using immunohistochemistry. Disruption of this epithelium, for example in inflammation or benign prostatic hyperplasia, may lead to some diffusion of the antigen into the tissue around the epithelium, and is the cause of elevated blood levels of PSA in this condition [11]. PSA is normally present in blood at low level, the desirable level of PSA that is considered normal in men is less than 4ng/ml [12]. Previous reports have shown that PSA level is increased in heavy metal toxicity [13,14]. The significantly raised PSA concentration in the e-waste exposed group in this study may be linked to a trend towards metal-induced oxidative stress and the associate initiation of carcinogenesis caused by the effects of heavy metals on the prostate tissue. Benign or cancerous tumor of the prostate has been reported to lead to excessive proliferation of the prostate cells including the epithelia cells of the prostate which are the site of production of PSA.

Pathological states in the prostate gland and reproductive system of the studied e-waste workers may arise from direct metal toxicity and and oxidative stress related conditions. Kampa et al. [15] demonstrated that testosterone induces PSA secretion by cells androgen sensitive human prostate adenocarcinoma cells (LNCaP) through membrane sites different from classical androgen receptors. Testosterone is produced by leydig and sertoli cell, with excessive proliferation of leydig and sertoli cells which may arise from tumor processes caused by DNA damage, induced by oxidative stress in heavy metal toxicity [15]. Under this condition testosterone secretion by the leydig cells will be increased. [15]. Testosterone has been shown to increase PSA secretion [15], thus increase in PSA level in the exposed subjects can also be linked to this mechanism.

Another mechanism for PSA increase in the exposed population may be associated with metal-metal interaction. WEEE-borne cadmium is known to be a metabolic antagonistic of zinc in biological systems. Some case-control studies have demonstrated that the concentrations of zinc in plasma/serum or total prostate tissue in men with Prostate cancer are lower than those in men without prostate disease or with benign prostate hyperplasia [16-18]. Superoxide dismutase contains zinc as a co-factor, therefore the unavailability of zinc in the prostate may result in reduced activity of SOD which will intensify oxidative stress and consequently DNA damage and tomogenesis in the prostate gland. DNA repair mechanisms defend against exogenous insults which can lead to gene rearrangement, translocation, amplification and deletion which in turn contribute to cancer development [19]. Zinc plays a vital role in these repair

mechanism through zinc finger [18,20]. Cadmium (found in WEEE) can antagonize zinc because cadmium and zinc have similar chemical properties. It has been suggested that even small repeated low doses of cadmium could accumulate and mimic zinc, leading to the adverse effects of cadmium observed on the prostate [21]. The occupational lifestyle our studied population showed near zero safety practices, a culture that predisposes the e-waste workers to toxic and carcinogenic chemicals (cadmium inclusive) in WEEE.

AFP value (3.56 ± 0.34 ng/ml) in e-waste exposed group was within the reference range of (3.04 ± 1.9 ng/ml) in healthy population. Howbeit, this value was significantly higher than the mean AFP levels in the unexposed group (2.14 ± 0.38 ng/ml).

Previous report demonstrated histopathological changes in liver of fish exposed to a wide range of heavy metals [22]. The value of testing for alpha-fetoprotein (AFP) for the diagnosis of primary hepatocellular carcinoma is well established [23,24]. The body has limited capacity to respond to cadmium exposure, as the metal cannot undergo metabolic degradation to less toxic species and it is only poorly excreted, making long term storage (especially in the liver) a viable option for dealing with this toxic element [22]. The increased AFP level in the exposed subjects of this study may be associated with the promotion of oxidative stress by liver-stored heavy metals, of which cadmium is a culprit being reportedly stored in the liver [22]. The oxidative stress stimulated in the liver by the accumulated heavy metals may cause DNA damage which may exacerbate cellular proliferation in the liver. The increased level of AFP may be attributed to this cellular proliferation.

Also, AFP reactivation in adults may result from liver regeneration, noncancerous liver diseases such as viral hepatitis or cirrhosis, primary liver or germ cell tumors and to lesser extent several forms of other epithelial malignances [25]. It is well known that the liver has regenerative ability; destruction of hepatocytes in heavy metal toxicity by oxidative stress will lead to stimulation of regeneration of hepatocytes which will consequently lead to increase in AFP as the expression of AFP gene is increased during growth and regeneration of the liver cells. This may have accounted for the higher AFP values obtained in the e-waste group.

In addition, AFP has been shown to be localized in the cytoplasm of hepatocytes, thus increased destruction of hepatocytes in heavy metal toxicity will reflect an increased level of serum AFP [25].

Thus, the rising AFP levels in the exposed participants of this study may be associated with the pathobiology of metal-induced hepatotoxicity in chronic occupational exposure.

Conclusion

This study concludes that the elevated cancer risk biomarkers (PSA and AFP) observed in the studied population of Nigerian e-waste workers may be associated with chronic and persistent occupational exposure to known carcinogens in e-waste. Use of personal protective devices and monitoring the status of PSA and AFP in Nigerian e-waste workers would be immensely useful. Unregualted importation and crude e-waste management practices should be discouraged in Nigeria and other developing countries.

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