

Lead and Cadmium in Public Health in Nigeria: Physicians Neglect and Pitfall in Patient Management

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Abstract

Low-level heavy metals exposure may contribute much more toward the causation of chronic disease and impaired functioning than previously thought. Among the suggested preventive and intervention measures for the control of renal diseases are the reduction in the exposure to heavy metals. Although these indicate knowledge and awareness of possible role of some heavy metals in the etiogenesis of some chronic diseases by Nigerian Physicians, heavy metal assay as diagnostic guide in patient management is often omitted in most healthcare settings. This is a synoptic capture of the increased incidence and prevalence of some metabolic disorders where heavy metals may be implicated. A search of the terms heavy metal exposure, source, toxicity, metabolic disorders, poisoning in Nigeria, in bibliographical databases (in English language) such as PubMed, Scopus, Google Scholar, and Africa Journal Online (AJOL) digital library was conducted. Leaded gasoline, refuse dumping, absence of poison information centers, and poor record keeping characterize environmental health in Nigeria. Lead and cadmium are of most significant public health importance in Nigeria. The recognition and inclusion of heavy metals assays in the diagnosis of metabolic disorders may ensure early diagnosis and improve management.

Keywords: Developing countries, Environmental health, Low-level metals, Metabolic disorders

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Introduction

Environmental contamination and exposure to heavy metals such as mercury, cadmium, lead, nickel, etc., is a serious growing problem throughout the world.^[1] Human exposure to heavy metals has risen dramatically in the past 50 years as a result of an expone increase in the use of heavy metals in industrial processes and products. In today's industrial society, there is no escaping exposure to toxic chemicals and metals. The level of metals in blood depends on the bioaccessibility rate^[2] and is considered as an index of biologically active metals in the body reflecting the environmental exposure of a population. Concentration of metal in blood is a

significant factor for public health.^[3] Studies conducted regarding the concentrations of metals in the blood and their relationships with environmental exposure provide useful information to the general public. Excessive dietary intake of lead was linked with cancers of stomach, small intestine, large intestine, ovary, kidney, lungs, myeloma, all lymphomas, and all leukemia.^[4]

The battle with communicable diseases, hygiene and other third world challenges has deemphasized health hazards posed by environmental heavy metals. Poisoning, whether acute or chronic, is not properly documented in Nigeria owing to poor record keeping.^[5] The symptomatic management of poisonings in most developing nations without Poison Information Centre has worsened the identification of heavy metals in spite of the fact that most developing nations like Nigeria live in a world awash with heavy metals^[6-19] [Table 1]. Lead and cadmium appear to be of more public health importance in Nigeria as shown in [Table 2].

In addition occurrence in food chain there are other sources of exposure to heavy metals in Nigeria. At the

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Table 1: Heavy metal pollution in Nigeria

Nigeria/ region	Pollution type/source	Pb	Cd	Mn	Cu	Co	Zn	Cr	Ni	As	Ref
Calabar	River sediment	20	0.2		64	15	184	65	67		Ntekim <i>et al.</i> , 1993 ^[6]
Ibadan	surface water	0.05	0.004		0.003	0.02	0.14		0.003		Mombeshor <i>et al.</i> , 1998 ^[7]
Nnewi	Soil	746		3617							Orisakwe <i>et al.</i> , 1999 ^[8]
Lagos	Soil	67.5-426	1.61-5.31								Fakayode and Onianwa, 2002 ^[9]
Osogbo	Soil	92.0	3.7		37.9		71.9		17.3		Fakayode and Olu-owolabi, 2003 ^[10]
Nigeria	Herbal medicines ^[1]	27	4.75			97.5	25.5		78		Obi <i>et al.</i> , 2006 ^[11]
Niger delta	Water	0.03- 0.06	0.01-0.11					0.03-0.08	0.03-0.09		Emoyan <i>et al.</i> , 2006 ^[12]
Niger delta	Fish	0.3	0.03					0.53	0.21		Oze <i>et al.</i> , 2006 ^[13]
Nigeria	Beverages	0.11	0.08								Maduabuchi <i>et al.</i> , 2006 ^[14]
Nigeria	Sachet water	0.04	0.04		1.40				0.05		Orisakwe <i>et al.</i> , 2006 ^[15]
Kano	Vegetable	13.19	0.74					12.89			Abdullahi <i>et al.</i> , 2007 ^[16]
Ogun	Fish	3.40	2.10		5.0		20.35			2.30	Farombi <i>et al.</i> , 2007 ^[17]
Awka	Drinking water	0.01	0.01	0.33				0.01	0.23	0.01	Nduka <i>et al.</i> , 2008 ^[18]
Awka	Vegetables	1.74	1.55	20.6				0.10	1.65	0.10	Nduka <i>et al.</i> , 2008 ^[18]
Awka	Food crop	0.10	0.10	0.10				0.77	0.10	0.10	Nduka <i>et al.</i> , 2008 ^[18]
Nigeria	Syrups	0.88	2.45								Orisakwe and Nduka, 2009 ^[19]

¹Values are expressed in mg/5 mL digested sample, All other values in the table are expressed as ppm (mg/L for water and mg/kg for others)

Table 2: Heavy metal blood levels in exposed and unexposed subjects

Group	BLL (ug/dl)	Cadmium (ug/dl)	Serum Nickel (ug/dl)	Chromium (ug/dl)	Reference
Nigeria/Port Harcourt	50.37±24.58 (41.40±26.85)				Alasia <i>et al.</i> , 2009 ^[26]
Nigeria/Nnewi	39.00±4.00 (17.00±4.00)	13.00±1.00 (9.00±2.00)	63.00±6.00 (25.00±4.00)		Orisakwe <i>et al.</i> , 2007 ^[21]
Nigeria/South West	63±9 (61±11)	62±13 (60±10)		61±7 (57±10)	Arinola <i>et al.</i> , 2008 ^[27]
Nigeria/South West	27.00±1.05 -48.90±19.1 (15.78±2.84) 4.6-130 ^s				Ademuyiwa <i>et al.</i> , 2005 ^[28] VanderJagt <i>et al.</i> , 2001 ^[30]

Control/unexposed values in parentheses, ^sBreast milk sample

top of the list are automobiles in the country, which still burn leaded gasoline. Although there was a plan to reduce the lead content of Nigerian gasoline from 0.74 to 0.15 g/L by 2002,^[20] there is no evidence to suggest that the program has been implemented. A large majority of automobiles on Nigerian roads are old second-hand vehicles built to run on lead gasoline, which have been imported from European countries. Newer vehicles designed to use lead-free gasoline have wasted their catalytic converters by burning leaded gasoline. Many vehicles are not well maintained and are driven on poorly maintained roads. As a consequence, a large

number of Nigerian vehicles characteristically emit blue plumes of bad odor and unburnt hydrocarbons,^[21] and release a higher percentage of the gasoline lead to the atmosphere.^[22] Other important sources of air-borne lead in urban areas of Nigeria include burning of garbage (containing domestic and industrial refuse, wood, paper products, plastics, discarded tires, battery casings, agricultural wastes, etc.) in open air (a common method of waste management), the use of wood fuel for cooking, and factories (including cottage industries) equipped with limited or no pollution control devices.^[23] After deposition, some of the contaminated dusts are cycled

back into the air, as evidenced by the trailing plume of dusts that accompany Lorries in many parts of Nigerian cities. The metal contaminated dusts become pervasively redistributed from the roadside^[24,25] to peoples' homes.

In a study to evaluate the degree of lead exposure and renal function tests in Port Harcourt, Nigeria, Alasia *et al.*^[26] found that occupationally exposed subjects had higher mean blood lead (B-Pb) $50.37 \pm 24.58 \mu\text{g}/\text{dl}$, than controls $41.40 \pm 26.85 \mu\text{g}/\text{dl}$ with a significant correlation with some renal function parameters. This study confirms earlier data presented by Orisakwe *et al.*^[27] and indeed other studies from different parts of Nigeria.^[28-30] [Table 2] The Nephrologist group of Alasia opined that level of environmental and occupational lead exposure in Port Harcourt, South-south, Nigeria is high, with occupational lead exposure increasing the risk of lead toxicity and renal function impairment.^[26] They concluded that lead exposure may be an overlooked risk factor for chronic kidney disease (CKD) in Nigeria and advocated that more studies be done and efforts be made to address the problem of lead exposure in Nigeria with the integration of these measures into preventive programs for CKD in Nigeria. Among the preventive and intervention measures cited by Alebiosu and Ayodele^[31] for the control of renal diseases, is the reduction in the exposure to heavy metals. Although these indicate knowledge and awareness of possible role of some heavy metals in the etiogenesis of some chronic diseases by Nigerian Physicians, heavy metal assay as diagnostic guide in patient management is often omitted in most healthcare settings.

This review is a synoptic capture of the increased incidence and prevalence of some metabolic disorders (hypertension, diabetes, renal disease, cancer, male infertility) in Nigeria of environmental importance. An attempt has been made as to what is expected by the regulatory agencies, scientists, and physicians for comprehensive management of chronic diseases (hypertension, diabetes, renal disease, cancer, male infertility) caused by environmental toxic burden.

An electronic and manual search of the terms 'heavy metal exposure, source, toxicity in Nigeria', 'metabolic disorders in Nigeria', 'poisoning in Nigeria' were performed through PubMed, Scopus, Google Scholar and Africa Journal Online (AJOL) digital library. Articles were not discriminated by date of publication. Data were extracted and compiled into tables that included heavy metal pollution in Nigeria and heavy metal blood levels in exposed and unexposed subjects. The search was restricted to mainly cases of hypertension, renal disease, diabetes, cancer, and infertility in Nigeria that implicated heavy metals. Studies also had to be published in English and conducted with human subjects in most cases.

Influence of heavy metals

In general, some heavy metals are systemic toxins with specific neurotoxic, nephrotoxic, fetotoxic, and teratogenic effects. Some heavy metals can directly influence behavior by impairing mental and neurological function, influencing neurotransmitter production and utilization, and altering numerous metabolic body processes.^[32,33] Accumulation of heavy metal, even at levels well below those considered nontoxic, can have serious health effects.^[34] Much of the damage produced by toxic metals stems from the production of oxidative free radicals, which in turn cause lipid peroxidation of biomolecules and fragmentation of deoxyribonuclei acid.^[35] Heavy metals disrupt a vast array of metabolic processes. They also alter pro-oxidant/antioxidant balance and bind to free sulfhydryl groups, resulting in inhibition of glutathione metabolism, numerous enzymes and hormone function.^[36] Nutritionally, heavy metals are directly antagonistic to essential trace elements and compete with nutrient elements for binding sites on transport and storage proteins, metalloenzymes and receptors. Disruption of the metabolism and balance of nutrient elements results in marked aberrations in the metabolism of carbohydrate, protein/amino acids, lipids, neurotransmitters, and hormones.^[37] Heavy metals can also increase the acidity of the blood and in effect, causes the body to draw calcium from the bones to help restore the proper blood pH. Furthermore, toxic metals set up conditions that lead to inflammation in arteries and tissues, causing more calcium to be drawn to the area as a buffer, contributing to hardening of the artery walls with progressive blockage of the arteries and osteoporosis. Even minute levels of toxic elements produce negative health consequences, affecting nutritional status, metabolic rate, the integrity of detoxification pathways, and the mode and degree of heavy metal exposure.^[38]

The biological half-lives for heavy metals are variably long; the half-life for cadmium in the kidney is decades. Most heavy metals are readily transferred across the placenta, found in breast milk, and are well known to have serious detrimental effects on behavior, intellect, and the developing nervous system in children.^[39] Andy *et al.*^[40] found that environmental cadmium exposure was associated with an increasing risk of all cause, cancer, and cardiovascular disease (CVD) mortality among men, but not among women. It is recommended that additional efforts be made to explain gender differences on the impact of environmental cadmium exposure. Kaori *et al.*^[41] reported that there were dose-response relationships between cadmium exposure and mortality risks in both male and female in the cadmium contaminated areas. Chronic exposure to cadmium could increase popular mortality and shorten life expectancy.

For adults, silent symptoms of chronic, low level heavy metal accumulation in tissues can progress from a steady decline in energy, productivity, and quality of life to accelerated CVD, premature dementia and total debilitation. Unfortunately, the possibility of heavy metal burden is often not considered.

Metals and male infertility

Some heavy metals like lead and cadmium could adversely affect the male reproductive system; either by causing hypothalamic-pituitary axis disruption or by directly affecting spermatogenesis, resulting in impaired semen quality.^[42,43] Several metals especially lead and cadmium are considered reproductive toxicants and/or suspected endocrine disruptor compounds. Jurasovic *et al.*^[43] reported positive associations between blood cadmium (B-Cd) concentrations and follicle stimulating hormone (FSH) and testosterone levels among men with no occupational exposure. Several studies have reported declines in semen quality associated with both lead^[44,45] and cadmium concentrations in blood.^[46] Other reports have shown an association between impaired sperm motility and cadmium and/or lead concentrations in sperm or seminal fluid.^[47,48] Taken together, studies suggest that the presence of lead and cadmium in the reproductive tract of men attending infertility clinics may be related to a moderate alteration of their seminal parameters.^[49]

Nigeria has about 12 million infertile persons.^[50] Although there is a general documented belief that the most common cause of infertility in Nigeria is infection,^[51] cases abound where infection have been treated without correction of infertility.^[50] In Nigeria there are higher rates of irreversible oligospermia or azoospermia than most other causes of infertility and less resources for the management of infertility.^[52] Of adult couples in African countries, it is estimated that 10-25% are subfertile and of these subfertile couples, female factors account for about 55% and male factors for about 30-40% of causes, whereas 5-15% of causes are unexplained.^[50]

Akinloye *et al.*,^[53] study in a Nigerian population, reported that high plasma cadmium level can be a cause of oligo-astheno-teratozoospermia syndrome. Preliminary result of an ongoing study in Nigeria showed that 83.97% of the patients with history of herbal intake had abnormal seminal fluid analysis, whereas only 16.03% of subjects with no history of herbal intake had abnormal results.^[54] This gives a clue of the possibility of male infertility from Nigerian herbal remedies, which has been reported to contain heavy metals.^[11] The reproductive health damage from consumption of Nigerian herbal remedies should be identified with indepth risk assessment.

Lead and cardiovascular diseases

In African populations, dyslipidemia as a risk factor for CVD and increasing incidents of death due to CVD in both urbanized and underdeveloped rural countries have been reported.^[55] There is also increasing evidence that environmental factors contribute to this dyslipidemia.^[56] Although cholesterol levels are lower in African population when compared with their American counterparts,^[57,58] the findings of Ademuyiwa *et al.*^[28] indicate that exposure to lead alters the metabolism of cholesterol and thus increases the risk of CVD and atherosclerosis in lead-exposed subjects. The cardiovascular effects of lead have been associated with increased blood pressure (BP) and hypertension. Studies in general populations have identified a positive association of lead exposure with coronary artery disease CAD and stroke mortality, and peripheral arterial disease.^[59,60] Cebi *et al.*^[61] found that mean levels of serum lead tended to be higher in CAD patients.

The precise mechanisms for the hypertensive effect of low chronic exposure to environmental lead are unknown. An inverse association between estimated glomerular filtration rate and B-Pb has been observed at B-Pb levels <50 µg/L in the general population,^[62] indicating that Pb-induced reductions in renal function could play a major role in hypertension. Other potential mechanisms include enhanced oxidative stress, stimulation of the renin-angiotensin system, and downregulation of nitric oxide^[63] and soluble guanylate cyclase.^[64] Effects on Na/K ATPase and on Ca²⁺ levels could also contribute to the effect on BP. These mechanisms could result in increased vascular tone and peripheral vascular resistance.

Cadmium and hypertension

Environmental exposure to cadmium increased total and noncardiovascular mortality in a continuous fashion without threshold.^[65] Cadmium may act on BP through mechanisms related to oxidative stress,^[66] endothelial dysfunction, and partial agonism of calcium channels, increased vasoconstriction, and activation of the sympathetic nervous system.^[67] It may also act through renal tubular damage, sodium retention, and volume overload.^[68] Only recently, Mordukhovich *et al.*^[69] found little evidence of associations between cadmium and BP but noted a cautious interpretation in the light of an unvalidated biomarker of exposure.

The annual medical reports of Nigeria from early 20th century to 1940s did not include hypertension in the lists of common CVDs, rather infection-related cardiac problems such as rheumatic heart disease, endocarditis, myocarditis, and pericarditis were most common.^[70] By the middle of the century, the prevalence of CVDs hitherto negligible increased to 11.2% in Nigeria^[71]

with hypertension becoming the most prevalent. A recent study by Adedoyin and Adesoye^[72] showed a prevalence of 32% (hypertension), 17.4% (stroke), 7.6% (cardiomyopathies), and 5.6% for other CVDs. The prevalence study of congestive cardiac failure done in Port Harcourt, the South-southern region of Nigeria implicated hypertension (56.3%) as the major cause with other disorders as cardiomyopathy, chronic renal failure, rheumatic heart disease, and ischemic heart disease accounting for 12.3%, 7.8%, 4.3%, and 0.2%, respectively.^[73]

Also, in a review of clinical profile of hypertension in Port Harcourt, 28.2% of all the medical admission was due to hypertension with its attendant complications ranging from stroke (39.9%), heart failure (22%), and renal failure (9.4%). The mortality rate due to the complications also followed the sequence with stroke (51.5%), as the major cause, and heart failure and renal failure accounting for 14.1% and 12.1%, respectively.^[74] Similar prevalence estimates have been documented in the literature. The incidence of CVDs in Uyo, South-southern state of Nigeria showed that hypertension accounted for (55.7%) of the cases, of these (34.4%) presented with cerebrovascular accident (CVA). About 44.3% presented with heart failure and causes included hypertension (14.9%), cardiomyopathies particularly the dilated type (15.1%), rheumatic heart disease (6.6%), and anemia (7.7%). Cardiovascular deaths (12.4%) were recorded, and of these (6.1%) were in patients with CVA.^[75]

In south-eastern Nigeria, prevalence of hypertension in a university community was as much as 21%.^[76] Arterial hypertension was found in 25% of examined motor bike riders in Benin City, Nigeria.^[77] It has been speculated that about 20–25% Nigerian adults could be classed as hypertensive.^[78] In Abeokuta, south-western state, the prevalence study also showed that hypertension (56.7%) was the major cause of cardiovascular disorders, followed by rheumatic heart disease (3.7%) and cardiomyopathy (3.0%). Other CVDs accounted for 4.4%.^[79] In north-western Nigeria, the highest incidence of CVD was seen between the age ranges of 40 and 49 years while the lowest incidence was seen between the age ranges of 19 years. A steady increase in the incidence of CVDs was also observed in north-western Nigeria from 2001 (14.1%) to 2005 (24.2%). CVD with highest occurrence was hypertension (39.1%) while congenital heart disease had lowest occurrence (1.1%). Hypertension had the highest occurrence of mortality (30.9%) while congenital heart disease had the lowest number of deaths (0.6%).^[80]

Lead and keratoconjunctivitis

Lead-induced retinal degeneration also appeared to be related to rod-specific effects of lead and calcium on rod

mitochondria, suggesting that lead and calcium bind to the internal metal-binding site of the mitochondrial transition pore, subsequently open the transition pore, and initiate the cytochrome C-caspase activation leading to apoptosis. These effects of lead on retinal cell apoptosis may have functional significance as long-term visual system deficits occur in humans, monkeys, and rats following low-to-moderate developmental exposure to lead.^[81] Lead causes irritations to the eye.^[82]

In their work on lead level in tear film among children with pollution keratoconjunctivitis (PKC) in the Niger Delta, Nigeria, Asonye and Bello^[83] showed that lead is present in concentrations, which cumulative effects could be devastating. Children usually are more vulnerable to exposure to pollutants in any environmental setting. A very small amount of a hazardous substance – an amount of no consequence elsewhere on the body – can be the cause of blindness to the eye.^[84] The high incidence of ocular irritations, lacrimation, photophobia, and specified conjunctival discoloration found among the sample population in Delta State may be associated with heavy metal pollution in these areas.^[83] With the increased industrial and exploratory activities in these areas, which are implicated as the sources of these environmental pollutants, the adverse effects of PKC can be expected to worsen. If this trend is not controlled, the levels of these pollutants in the tears are expected to increase, further triggering PKC.

Cadmium in nephrotoxicity

Based on toxicological studies, the researches on human specific-injury caused by cadmium exposure have focused on injury biomonitoring of bones and urogenital system.^[85] Mainline studies on cadmium toxicities were early screening for the early sensitive biomonitoring indices, monitoring and evaluation of target organ damage, and study on the dose-response relationship between cadmium exposure and health damage indices.

There were a lot of early indices of kidney damage applied in the popular surveys. Some were related to body burden of cadmium exposure, such as B-Cd and urinary cadmium (U-Cd); Some were sign of bone injury, such as bone mineral density (BMD), urine calcium, urine phosphorus, urine or serum alkaline phosphatase (U-, B- ALP), urine hydroxyproline (U-HOP), and so on. Index commonly used to show cadmium accumulation level in renal cortex and the whole body was U-Cd. There are generally two different kinds of groups of biomonitoring indices for renal tubular dysfunction and renal tubular pathological damage: urine protein and urine enzyme. The most commonly used indices were U-Cd, U β 2-MG (urine β 2-micro-globulin (U β 2-MG), and U-NAG (N-acetyl- β -D-glucosaminidase (U-NAG)

(U-NAG applying in three ways: A-isozyme, B-isozyme, and total NAG, renal tubular epithelial cells are rich in B-NAG), among which good correlations have been observed.^[85]

With increase in cadmium exposure level, U-Cd, urine enzyme, and urine protein would be synchro-increasing, showing signs of renal tissue injury with renal dysfunction.^[85] The renal tubular injury induced by environmental cadmium exposure has been found to be irreversible even after soil replacement in cadmium-polluted rice paddies.^[86] In the late stage of cadmium exposure, it has been seen that U-Cd and urinary protein increased sharply with urinary enzyme reduction. Proactive measures should be taken to control environmental cadmium to prevent cadmium health damage.

Cadmium and diabetes

Schwartz *et al.*^[87] published a large cross-sectional human study in which they reported a significant positive relationship between U-Cd, impaired fasting glucose, and diabetes, suggesting that cadmium exposure plays a role in diabetes etiology. Renal damage could cause cadmium to leak into urine, potentially leading to a (noncausal) association between cadmium and diabetes. The investigators therefore restricted the analysis to persons without evidence of renal damage, but this restriction did not appreciably affect their findings. There were clear dose-response relationships between U-Cd and fasting glucose as well as diabetes. However, the pathogenesis remains to be explored. But using monkeys, Kurata *et al.*^[88] showed that cadmium accumulates in the pancreas and that chronic exposure initiates degeneration of islet cells and induces the clinical signs of diabetes. Cadmium exposure also potentiates some diabetic complications related to renal tubular and glomerular function.^[89]

Over the past 30 years, the prevalence of diabetes in Nigeria has been increasing steadily. In 1971, a hospital survey by Osuntokun *et al.*^[90] in Ibadan estimated a prevalence of 0.4%, while Owoaje *et al.*^[91] found a prevalence of 2.8% in Ibadan. In 1988, while screening for diabetes during a World Diabetes Day in Lagos metropolis, Ohwovoriole *et al.*^[92] found a prevalence of undiscovered diabetes of 1.6%. A national survey in 1992 by the Noncommunicable Disease Expert Committee of the Federal Ministry of Health recorded a prevalence of 2.2% (National) – Lowest 0.5% in Mangu, Plateau State and highest 7% in Lagos Island. A survey by Puepet,^[93] in urban adults in Jos metropolis, discovered a prevalence of undiscovered diabetes to be 3.1%; By 2004, a second survey in Jos recorded a prevalence of 10.3%. In Ekpoma, South-southern Nigeria, a prevalence

of 9.8% was recorded among University staff.^[94] In the early 1990s, diabetes was almost unheard of, but from the mid 1990s till date, the prevalence has been on the increase. Although some researchers have attributed this to nutritional transition and sedentary lifestyle, it is feared that heavy metals may be on top of the list of causative factors.

Cadmium and cancer

With some patients presenting with hormonal disorders in many hospitals today, it could be apparent that the contamination of the environment with heavy metals, which act as metalloestrogens, for example, cadmium, has contributed to the disruption in endocrine system. It has been shown that low dose cadmium exposure has potent estrogen and androgen-like activities by directly binding to estrogen and androgen receptors (ARs).^[95] More importantly, at a dose similar to the World Health Organization Provisional Tolerable Weekly Intake, cadmium mimics the *in vivo* effects of estrogen in target organs in animal studies.^[95]

The prominence of estrogens in the etiology of breast cancer suggests that environmental exposures that mimic the effects of estrogens may be potential risk factors for the disease. The growth and development of the prostate gland is under the control of androgenic sex steroids. The effects of androgens on the expression of genes involved in the growth as well as in the secretory function of the gland are mediated by the AR. In addition to normal growth and function, androgens play a central role in the development of prostate cancer, and a low dose cadmium exposure has been shown to have androgen-like activity on ARs.^[95]

Several studies suggest that exposure to cadmium is a risk factor for the development of prostate cancer. Martin *et al.*^[96] found that prostate cancer was associated with dietary exposure to cadmium through drinking water and food.

In Nigeria, the incidence and prevalence of cancer has been on the increase. This was revealed by the data released by the Kano Cancer Registry.^[97,100] From the profile, cancers of the cervix (22.9%), breast (18.9%), ovary (8.2%), nonmelanoma skin cancer (6.3%), and uterus (6.2%) were the most frequent female cancers. In males, cancer of the prostate (16.5%), bladder (10.2%), nonmelanoma skin (9.9%), colorectum (9.3%), and connective tissue (6.3%) were most common. Burkitt's lymphoma (31.4%), other lymphoreticular cancers (23.8%), and retinoblastoma (20%) predominated in children.^[97] In recent times, cancer has emerged as a major public health problem in many developing countries, matching its effect in industrialized nations. Already, the WHO notes in the 2008 World Cancer

Report that there are 100,000 new cancer cases in Nigeria each year and only the adoption of healthy lifestyles by the populace, and concerted public health action could reduce the tide. It is estimated that by 2020, cancer incidence for the males and females in Nigeria may rise to 90.7/100,000 and 100.9/100,000, respectively. It is also projected that by 2020, death rates from cancer in Nigerian males and females may reach 72.7/100,000 and 76/100,000, respectively.

Cadmium and osteoporosis

Cadmium is also a known risk factor for osteoporosis, reportedly causing osteomalacia followed by osteoporosis at high concentrations. A number of epidemiological and experimental studies have been conducted to evaluate the relationship between cadmium exposure and the development of bone diseases.^[98] Recently, the incidence of osteoporosis has been rapidly increasing worldwide. There are many risk factors for osteoporosis ranging from environmental chemical substances to hormonal effects. Exposure to cadmium and fluoride ions is one of the environmental risk factors associated with osteoporosis.

In Nigeria, the prevalence of dental problems has been on the increase. The causes of teeth loss among Nigerians showed periodontal disease (46.4%) and dental caries (43.9%) as the major causes with trauma (4.5%), tooth impaction (2.4%), and orthodontic problem (1.6%) as the least cause.^[99]

Recommendations for further research

Much work is needed to realize metal health risk in a developing country such as Nigeria. Future research thrust should be aimed at:

- i. Conducting follow-up study on health hazards of all kinds of people, evaluate the population metal exposure and the severity of health damage related, and analyze its trend;
- ii. Concern about the human disease and death impact due to metal exposure, collect and screen the information of population disease and death closely related to metal exposure, and study the link and dose-response relationship between organ damage and metal exposure;
- iii. Establishing human health hazard monitoring and early warning network of metal exposure in the framework of environmental public health monitoring;
- iv. Implementing prevention and intervention research on population health hazards of environmental metal exposure to reduce the risk of population metal exposure and health injury related. The few studies undertaken so far to estimate the impact of heavy metals on these health changes in Nigeria in spite of the rising trend speak loud of the information gap and challenge to researchers;

Summary

An individual with metals toxicity, even if high dose and acute, typically has general symptoms, such as weakness or headache. This makes the diagnosis of metals toxicity in a clinical setting very difficult unless a clinician has the knowledge and training to suspect the diagnosis and is able to order the correct diagnostic test. Chronic exposure to metals at a high enough level to cause chronic toxicity effects (such as hypertension in individuals exposed to lead and renal toxicity in individuals exposed to cadmium) can also occur in individuals who have no symptoms. These technicalities in proper diagnosis of heavy metal toxicity demand special training for physicians in developing nations like Nigeria given the unregulated exposure. Much about metals toxicity, such as the genetic factors that may render some individuals especially vulnerable to metals toxicity, remains a subject of intense investigation. It is possible that low-level metals exposure contributes much more toward the causation of chronic disease and impaired functioning than previously thought.^[100]

It is required in practice therefore that, clinicians should identify patient's current exposure and toxic load compared with standard guideline averages (since national averages are not available in Nigeria) and monitor the effectiveness of prescribed treatments. There should be a refocusing on treating chronic diseases caused by environmental toxic burden. Research and regulatory bodies should provide unique exposure information to scientists, physicians, and health officials to help prevent diseases due to some environmental chemicals. The recognition and inclusion of heavy metals assays in the diagnosis of metabolic disorders will definitely improve management.

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