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Renal Function Assessment in Adults with Occupational Heavy Metal Exposure in Yenagoa, Bayelsa State, Nigeria

Ujah Terhide[1], Ndu O. Victor[1], Ogenyi Timothy[1], Alasia Dennis[2], Egbi Oghenekaro[3]

[1]Department of Internal Medicine, Federal Medical Centre, Yenagoa, Bayelsa State
[2]Department of Internal Medicine, University of Port Harcourt Teaching Hospital (UPTH), Rivers State
[3]Department of Internal Medicine, Niger Delta University Teaching Hospital (NDUTH)

ABSTRACT

Background: Heavy metal exposure has been associated with numerous health effects including renal involvement. The exposure to heavy metals is still notably prevalent, and possibly on the rise particularly in some occupations. Crude oil exploration and other related industrial activities could be a contributory factor in some regions.

Objectives: The study aimed to determine the level of blood heavy metals (lead and cadmium) and the renal function of occupationally exposed persons in Yenagoa as compared to others with less probable risk of heavy metal exposure.

Method: Three hundred and ten (310) adults (157 study participants and 153 controls of similar age and sex) aged 18 years and above were recruited for the study via simple random sampling. The participants included smelters, auto-mechanics, vulcanizers, artisan refinery workers and petrol station attendants with each occupation categorized as clusters and non-proportionate allocation of participants for each cluster who met the inclusion criteria. The control group consisted of individuals in other occupations with less probable risk of exposure. The participants were evaluated for Urinalysis, Serum Creatinine, Haemoglobin, blood lead and cadmium. The outcome was analyzed using version 25.0 of Statistical Package for Social Sciences (SPSS) software.

Results: A total of 310 participants took part in the study with 235 (75.8%) males and 75 (24.2%) females with a male to female ratio of 3.1:1. The mean age of the study population was 35.6 ± 10.7 years. The mean level for lead and Cadmium was 48.29 ± 26.29µg/dl and 4.56 ± 3.07µg/l respectively which was higher than that of control (Pb - 27.42 ± 11.17µg/dl, Cd - 2.65 ± 1.62 µg/l). The mean eGFR was significantly lower in the exposed population, 77.39mls/min/m2as compared with control (82.57mls/min/m^2). The mean haemoglobin level was also significantly lower in the exposed populations as compared with the controls.

Conclusion: This study shows elevated levels of serum heavy metals in the occupationally exposed individuals with probable impact on their renal function in the Niger Delta region of Nigeria when compared to their non- exposed counterparts. There is a need for occupational health education to help in the prevention of excessive heavy metal exposure and curb its impact on health of all involved.

INTRODUCTION

Heavy Metals are poorly defined elements with a mass density greater than 4.5g/cm^2 which tend to release electrons in chemical reactions and form simple cations. They include copper (Cu), Cobalt (Co), Chromium (Cr), Cadmium (Cd), Iron (Fe), Zinc (Zn),

Corresponding author: **Ujah Terhide,** Department of Internal Medicine, Federal Medical Centre, Yenagoa,
E-mail: terhideujah@gmail.com

Lead (Pb), Mercury (Hg), Manganese (Mn), Nickel (Ni) and Mobydellum (Mo). They are generally classified as physiologically active or inactive [1].

Their common characteristic toxic property is that they dissociate well and are easily soluble because they can penetrate through cell membranes and get into internal organs like kidneys, adrenals, liver, lungs and skin causing various health effects including toxic nephropathy [1].

The main threats to human health from heavy metals are associated with exposure to arsenic, lead, cadmium and mercury. Exposure to these metals are common in both domestic and industrial settings [2].

The sources of contamination or pollution of the environment by heavy metals include different branches of industry, power, transport, mineral waste management and fertilizers. The World Health Organisation (WHO) has created guidelines with respect to expected exposure levels however these guidelines are hardly adhered to especially in developing countries [3].

In Nigeria, for instance, the Niger- Delta region has high levels of petroleum exploration and refining activities as well as other industrial activities associated with heavy metal contact. These activities constitute the livelihood of many of the occupants of these regions so continuous exposure is inevitable with consequent adverse health impact [4].

The health effects of heavy metal exposure are multisystemic with renal involvement being commonly reported. However systematic studies of toxic nephropathy are yet to adequately establish cause- effect relationship [5]. This study aims to fill the gap.

In Nigeria, occupational heavy metal exposure in Nigeria is notably prevalent and uncontrolled [4]. Its importance as both an association and/or cause of renal dysfunction has been under-studied in Nigeria.

In addition to well documented occupational exposure, southern Nigeria is known particularly for illegal mining and oil exploration activities making it a likely highly contributory factor to nephrotoxicity [6].

The objective of this study was to determine the level of blood heavy metals and the renal function of occupationally exposed persons in Yenagoa as compared with non - exposed counterparts.

METHOD

The study was carried out on adults who were 18 years above working as petrol station attendants, auto-mechanics, artisan refinery workers, vulcanizers and smelters in a semi-urban community, Yenagoa in Bayelsa State, Nigeria. The control population consisted of adults of similar age and sex not involved in the stated occupations and possibly lesser risk of occupational and they included civil servants, teachers and traders. Participants with hypertension, diabetes or established kidney diseases from other causes were excluded from the study.

Ethical approval for the study was obtained from the research committee of the Federal Medical Centre, Yenagoa. All participants were informed concerning the purposes of the research and achieved the printed consent.

Before samples collection, each individual had an extensive interview by the primary researcher with the aid of trained research assistants who filled a structured questionnaire about their possible diseases and dietary habits. Information on job experience, socioeconomic situations like income and education, and history such as drug uses smoking and alcohol consumption were acquired from questionnaires and every worker was interviewed by a trained interviewer.

Blood samples were collected for serum haemoglobin, creatinine and blood cadmium and lead levels. Mid-stream urine was also collected and assessed for protein using dipstick strips.

A venous blood sample (8-10mls) was collected from the Brachial vein of the ante-cubital fossa maintaining asepsis in each participant. Blood sample (2mls each) was placed in EDTA bottle and lithium heparin bottle for haemaglobin, glucose and creatinine estimation respectively. Then the remaining blood sample was put in plain bottle for blood heavy metals (lead and Cadmium) estimation.

The serum haemoglobin was estimated using the Cyan methaemoglobin method; serum creatinine was measured by the Jaffe kinetic method.

The eGFR was calculated from the standardised creatinine by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[7].

The serum concentrations of lead and cadmium were estimated with the use of graphite furnace Atomic Absorption Spectroscopy. Standard graphite tubes were used for the determination of lead and pyrolytical graphite tube for the determination of cadmium [8].

Urine samples were collected in universal bottles for qualitative protein estimation using dipstick method.Proteinuria was measured using reagent strips. A test result of 1+ or higher was defined as being positive.

STATISTICAL ANALYSIS

Statistical Package for Social Sciences (SPSS) software version 25.0 was used for data cleaning and analysis. Variables were presented in tables and figures as appropriate. Differences in the distribution of categorical variables between the exposed and the control groups were investigated using the Chi- square test of proportion. The mean serum level of heavy metals in both groups was estimated and the difference in the mean values of lead and cadmium in the exposed and control groups was tested using the students' t-test.

The difference in mean eGFR between the exposed and control group and between the different occupational groups was assessed by the student's t-test and the analysis of variance respectively.

Level of statistical significance was set at p-value < 0.05.

RESULTS

A total of 310 participants took part in the study with 157 occupationally exposed and 153 controls. The participants include 235 males and 75 females, with a male to female ratio of 3.4:1. The mean age of the study population was 36.2 (± 10.4) years. Table 1.

Most of the study participants were married. In the exposed population, secondary level of education (56.7%) and the mean duration of occupation in the exposed category in this study was 12.3 ± 10.6 years. Table 1

Table 1: Sociodemographic and Occupational Duration of Study Participants

Characteristics	Study Categories			Test Statistics	p-value
	Total N = 310 (%)	**Exposed N = 157 (%)**	**Control N = 153 (%)**		
Sex					
Male	235 (75.8)	120 (76.4)	115 (75.2)	0.07a	0.794
Female	75 (24.2)	37 (23.6)	38 (24.8)		
Age group					
< 30 years	103 (33.2)	55 (35.0)	48 (35.0)	0.68a	0.878
30 - 39 years	82 (26.5)	40 (25.5)	42 (27.5)		
40 - 49 years	85 (27.4)	41 (26.1)	44 (28.8)		
≥ 50 years	40 (12.9)	21 (13.4)	19 (12.4)		
Mean Age (SD) in years	36.2 ± 10.4	35.6 ± 10.7	36.9 ± 9.9	1.16b	0.248
Marital status					
Single	101 (32.6)	65 (41.4)	36 (23.5)	11.27a	0.001*
Married	209 (67.4)	92 (58.6)	117 (76.5)		
Educational level					
No formal education	3 (1.0)	3 (1.9)	0 (0.0)	139.67a	0.001*
Primary education	47 (15.2)	45 (28.7)	2 (1.3)		
Secondary education	121 (39.0)	89 (56.7)	32 (20.9)		
Tertiary education	139 (44.8)	20 (14.4)	119 (77.8)		
Duration of work exposure in years	11.1 ± 9.5	12.3 ± 10.6	9.9 ± 8.8	2.23b	0.026*

**Statistically significant; [a]Chi-square test; [b]Student's t test; SD Standard Deviation*

BLOOD LEVELS OF HEAVY METALS IN STUDY PARTICIPANTS

Comparison of levels of heavy metals in 'exposed' and 'control' group

Blood levels of heavy metals {Lead (Pb) and Cadmium (Cd)} was assessed within 5 occupations; mechanics, smelters, vulcanizers, smelters and petrol station attendants and compared with controls.

In table 2, the mean lead level in the exposed population was 48.29 ± 26.29µg/dl while the value in the control population was 27.42 ± 11.17µg/dl and this was statistically significant (p-value - 0.001). Within the exposed populations, lead levels were highest among the Artisan refinery workers, 58.11 ± 25.55µg/dl followed by the Petrol Station Attendants, vulcanizers, smelters, and mechanics accordingly.

Cadmium levels was also higher in the exposed population, (a mean level of 4.56 ± 3.07µg/l than in the control participants 2.65 ± 1.62µg/l) and this was statistically significant with a p-value of 0.001. In the exposed population, Cd was highest in the vulcanizers 6.61 ± 3.72µg/l, then, mechanics, artisan refinery workers, smelters and petrol station attendants respectively. Table 2

Table 2: Blood level of heavy metals among study participants

Study groups		Lead		Cadmium	
		Mean ± SD	Significant test (p-value)	Mean ± SD	Significant test (p-value)
Total	310	38.07 ± 22.78		3.59 ± 2.70	
Study groups					
Exposed	157	48.29 ± 26.29	8.97a (0.001)	4.56 ± 3.07	6.81 (0.001)
Control	153	27.42 ± 11.17		2.65 ± 1.62	
Occupational groups					
Mechanics	32	29.78 ± 17.14	28.36b (0.001)	4.95 ± 3.27	17.33 (0.001)
Smelters	31	46.03 ± 26.11		3.91 ± 3.11	
Petrol station attendants	30	56.41 ± 21.32		2.98 ± 1.28	
Artisan refinery workers	33	58.11 ± 25.55		4.09 ± 2.91	
Vulcanizers	31	52.17 ± 29.85		6.61 ± 3.72	

[a]Students t-test, [b]F-test result from ANOVA

Heavy Metals Levels in the 'Exposed' group according to Occupation Duration

The mean level of lead among participants in the exposed group who have worked for less than 10 years was 42.20 ± 26.06µg. For participants who have worked for 11 - 20 years, 21 - 30 years and 31 - 40 years, the mean serum level of lead was 42.41 ± 29.42 µg; 43.19 ± 23.86 µg; 51.93 ± 22.40 µg respectively (Figure 1). Participants who have spent 30 - 40 years in the exposed group had significantly (f -test = 3.18; p - 0.026) higher mean serum values than those who have spent less than 30 years.

Figure 1 also shows that Cadmium followed a similar trend to lead, with mean values of 4.32 ± 2.85µg, 4.33 ± 4.01µg, 4.28 ± 2.56 µg and 5.60 ± 5.63 among participants who were less than 10 years, 11 - 20 years, 21 - 30 years and 31 - 40 years respectively. However, there was no significant difference (f-test = 1.05; p - 0.373)in the level of serum cadmium in the different work duration categories.

Renal Function of Exposed Participants

Comparison of renal function among 'exposed' and 'control' group

The renal function of participants was estimated as shown in Table 3. The mean eGFR of the exposed participants was 77.28mls/min/m^2 and was lower than that of control (82.71mls/min/m^2) with a p-value of 0.007. The vulcanizers also had the least mean eGFR (73.16), followed by the petrol station attendants, smelters, artisan refinery workers and mechanics accordingly.

The mean haemoglobin concentration among the exposed was 12.8±1.4 g/dl and was lower than that of the control group, 14.5±1.7 g/dl. This is statistically significant with a p-value of 0.001. Table 4.

Proteinuria was observed in 5 (1.9%) participants among the exposed and 2 participants in the control with a p-value of 0.448.

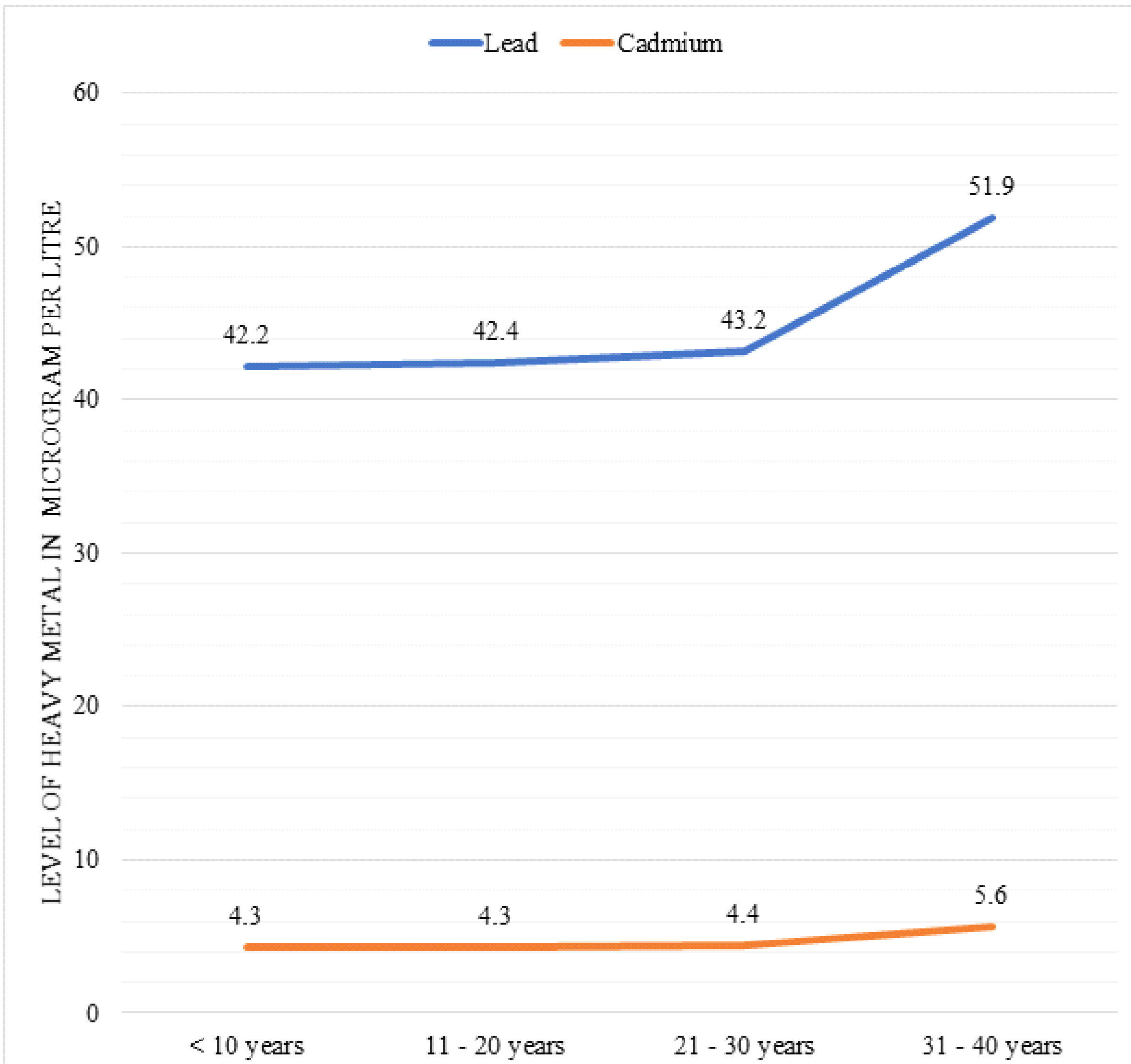

Figure 1: Line graph showing heavy metals levels of the occupationally exposed in relation to the work duration *(f-test = 3.18; p - 0.026 for Serum Lead; and f-test = 1.05; p - 0.373 for serum Cadmium)*

Table 3: Estimated glomerular filtration rate (eGFR) of participants

Study group	Total	Mean eGFR	Standard deviation	Test Statistics	p-value
Total population	310	79.96	16.84		
Study Group					
Exposed	157	77.28	13.98	2.73a	0.007*
Control	153	82.71	19.00		
Occupation					
Mechanics	32	81.06	16.74	2.55b	0.028*
Smelters	31	77.52	12.42		
Petrol Station Attendants	30	74.50	15.32		
Artisan refinery workers	33	79.79	12.77		
Vulcanizer	31	73.16	11.11		

**Statistically significant; [a]Student's t test; [b]ANNOVA; eGFR estimated Glomerular Filtration rate*

Table 4: Haematological and Biochemical Indices of study participants

Characteristics	Total	Study Categories		Test Statistics	p-value
		Exposed	Control		
Laboratory findings					
Haemoglobin Concentration	13.7 ± 1.8	12.8 ± 1.4	14.5 ± 1.7	9.62a	0.001*
Serum Creatinine	108.2 ± 21.5	111.5 ± 19.5	104.1 ± 21.1	3.25a	0.001*
Protein in Urine					
Yes	7 (1.6)	5 (1.9)	2 (1.3)	1.23b	0.448
No	303 (98.4)	152 (98.1)	151 (98.7)		

**Statistically significant; [a]Student's t test [b]Chi-square test;*

DISCUSSION

This was a cross sectional study consisting of 157 participants who were 18 years and above working as auto mechanics, vulcanizers, artisan refinery workers, petrol station attendants and smelters and 153 controls in other occupations with less probable exposure.

There was male preponderance with a ratio of 3.4:1 due to the peculiarities of occupations studied and this is similar to studies in Nigeria by Alasia et al and Anetor *et al* [4,9]. The reason for male preponderance is due to the physically demanding and highly time-consuming nature of most of the occupations. The mean age of the participants was 35.6±10.7 years which is similar to 31.66±7.74 years by Wang *et al* and Yakubu *et al* [10,11] but slightly lower than 41.2±8.3 years by Ehrlich *et al* and 46.9±14.5 years by Reilly *et al* [12,13]. The probable reason for the age difference is that most likely the fact that these latter studies covered extensive geographical regions; so recruited participants with longer duration of exposure and work experience. The mean duration of occupational exposure in this study was 12.3±10.6 years and this was similar to 16.7±2.13 years by Anetor *et al* [9] in Southwest Nigeria and 11.6 years among battery factory workers in South Africa by Ehrlich *et al* [12] but lower than 27.7±7.3 years by Roels *et al* [14]. The probable difference is that the least occupational duration for participants in the latter study was 6 years unlike the index study with a year of exposure as least occupation duration.

The mean level of lead in this study was 48.29±26.29µg/dl among exposed participants which was similar to 50.37±24.58 µg/dl by Alasia *et al* [4] in Port Harcourt and 43.5µg/dl among roadside automobile technicians by Saliu *et al* [15] in Lagos

Nigeria. The levels were higher than 16.0µg/dL by Kassy *et al* [16] the probably difference was that this study assessed only one occupation (auto body mechanics) and had a larger sample size. The lead levels were slightly higher in a study carried out by Dioka *et al* [17] in South East Nigeria, this is probably due to a small sample size one occupation (artisans) assessed unlike the index study of different occupations with varied levels of exposure. However, in all the aforementioned studies, lead level was higher in exposed study participants as compared with controls. This trend is similar internationally as seen in Battery factory workers in China by Zhang *et al* [18] and Potters in Brazil by Bandeira *et al* [19] as significantly higher levels of lead as compared to controls. A meta- analysis carried out by Kuraeiad *et al* [20] on blood lead level and renal impairment observed significant difference in blood levels in exposed more than their counterparts with lesser risk of exposure.

The mean serum Cadmium level was 4.56±3.07µg/l in the exposed participants and was significantly higher than that of controls 2.65±1.62µg/l and this is similar to studies carried out by Adewale et al in Abuja, [21] Orisakwe et al [22] in South East, Nigeria and Yakubu *et al* [11] in Jos. This trend of significantly elevated cadmium levels in occupationally exposed compared to controls was also observed internationally by Goyal *et al* [23] in India andin a cadmium smelting factory in China by Zhou *et al* [24]. Varied mean cadmium levels were noticed in these studies and these were mainly accounted for by nature of occupations involved and level of exposure. However, occupationally exposed group levels of cadmium were significantly higher than controls. The mean heavy metal levels were also noticed to be increased as work duration increases, this proportional trend was also noticed in studies by Assadi *et al* [25] Roels *et al* [14] Zhou *et al* [24] and Yu *et al* [26]. This probably indicates increased tissue levels with prolonged exposure.

The mean eGFR of the exposed participants was 77.39mls/min/m^2 which was lower than control, 82.57mls/min/m^2 and this was statistically significant. The possible reason for the lower eGFR is likely from the tubular damage of heavy metals on the kidneys. This is similar to findings from studies carried out Yakubu *et al* [11] in Jos and in an oil and gas flaring communities in Imo state by Egwurugwu *et al* [27]. However, renal function was not significantly affected in study carried out by Aneto *et al* [9]. This is probably due to comparably less extensive nature of study. Studies by Yu *et al* [26] and Roels *et al* [14] also indicated no effect in renal function in occupationally exposed. These observations are undergoing further evaluations.

Internationally, Reilly *et al* [13] observed in smelting community in Dallas that for each unit increase in blood lead, there was a corresponding decrease in eGFR and Kuraeiad et al [20] observed increased creatinine (and reduced creatinine clearance) in lead - exposed compared to non- exposed participants.

The prevalence of persistent proteinuria in this exposed population was 1.9% and this was not statistically significantly increased from that of control. This is similar to studies by Aneto [9] that indicated increased in urinary microalbumin levels in the occupationally exposed but not statistically significant from that of controls. This prevalence was lower than 10.3% by Tsai *et al* [28]. The difference is probable due to fact that other risk factors such as hypertension and DM where not excluded in the study.

Serum haemoglobin in the exposed participants was significantly lower than that of the control subjects most likely from the effect of heavy metals such as lead on red cell oxidation and bone marrow suppression. This is similar to studies carried by Saliu *et al* [15] in Lagos and Chukwukasi et al in South East Nigeria [29]. Despite differences in the mean haematological parameters in the comparism groups, most of the participants had blood levels of haemoglobin within the normal range. Hsieh *et al* [30] observed that cumulative exposure to lead at workplace was significantly associated with anaemia risk among Taiwan workers. Basit *et al* [31] reported presence of anaemia in heavy metal exposed battery workers in Parkistan unlike in the control group indicating haematologic changes occurring from long term exposure to heavy metals. However, Froom *et al* [32] observed that haemoglobin levels did not correlate with blood lead levels in battery workers in Israel. The possible reason for the difference is most likely due to low prevalence of elevated heavy metals in the latter study with subsequent probable less effect on haematologic parameters.

Cohort studies on lead exposed workers in United States of America, Finland and United Kingdom (UK) by Steenland *et al* [33] found positive trends for renal damage and other co-morbidities and mortality associated with increasing blood lead levels. Madrigal *et al* [34] also observed that cadmium exposure was associated with decreased glomerular filtration and increased urine protein excretion.This study further reiterates the emerging concerns of heavy metals and its effects on renal function and other health concerns.

This study however did not assess urinary levels of heavy metals or tissue levels such as bone lead levels which are significant markers heavy metal exposure [35,36].

The study however suggests a probable effect of heavy metals on renal function after exclusion of other common risk factors such as diabetes and hypertension. The need for adequate health education and improved work regulation cannot be over-emphasized.

REFERENCES

1. Szyczewski P, Siepak J, Niedzielski P, Sobczy?ski T. Research on Heavy Metals in Poland. 2009;18(5):755-768.
2. Sabath E, Robles-osorio, Ludivina M. Renal health and the environment?: heavy metal nephrotoxicity. Spanish Nephrol Soc. 2012;32(3):279-286.
3. Morais S, Garcia E Costa F, Pereira M de L. Heavy Metals and Human Health. In: Oosthuizen PJ, editor. Environmental Health - Emerging Issues and Practice. Intech Open Science; 2012; 227-243.
4. Alasia D, Emem-Chioma P, Wokoma F. Association of Lead Exposure, Serum Uric Acid and Parameters of Renal Function in Nigerian Lead- Exposed Workers. Int J Occup Environ Med. 2010;1(4):182-190.
5. Chapman E, Haby MM, Illanes E, Sanchez-Viamonte J, Elias V, Reveiz L. Risk factors for chronic kidney disease of non-traditional causes: a systematic review. Rev Panam Salud Pública. 2019;43(e35):1-12.
6. Kadafa AA. Oil Exploration and Spillage in the Niger Delta of Nigeria. Civ Environ Res. 2012;2(2):38-51.
7. Spector JT, Navas-Acien A, Fadrowski J, Guallar E, Jaar B, Weaver VM. Associations of blood lead with estimated glomerular filtration rate using MDRD, CKD-EPI and serum cystatin C-based equations. Nephrol Dial Transplant. 2011;26 (9):2786-2792.
8. Fewtrell L, Kaufmann R, Prüss-Üstün A, Campbell-Lendrum D, Corvalán C, Woodward A. Lead Assessing the environmental burden of disease at national and local levels World Health Organization Protection of the Human Environment Geneva 2003. WHO Enviro. Geneva: World Health Organization; 2003. 1-73.
9. Anetor JI. Serum uric acid and standardized urinary protein: Reliable bioindicators of lead nephropathy in Nigerian lead workers. African J Biomed Res. 2002;5(1-2):19-24.
10. Wang X, Liang H, Wang Y, Cai C, Li J, Li X, et al. Risk factors of renal dysfunction and their interaction in level-low lead exposure paint workers. BMC Public Health. 2018;18(1):526.
11. Yakubu B, Harrison U N, Dennis C N, Olaniru B O, John I, Bot YS. Lead and Chromium in Artisans and Petrol Hawkers in Jos, Nigeria. Int J Nephrol Kidney Fail. 2020;6(1):1-6.
12. Ehrlich R, Robins T, Jordaan EE, Miller S, Mbuli S, Selby P, *et al*. Lead absorption and renal dysfunction in a South African battery factory. Occup Environ Med. 1998; 55(7): 453-460.
13. Reilly R, Spalding S, Walsh B, Wainer J, Pickens S, Royster M, *et al*. Chronic environmental and occupational lead exposure and kidney function among African Americans: Dallas lead project II. Int J Environ Res Public Health. 2018;15(2875):1-10.
14. Roels H, Lauwerys R, Konings J, Buchet JP, Bernard A, Green S, *et al*. Renal function and hyperfiltration capacity in lead smelter workers with high bone lead. Occup Environ Med. 1994;51(8):505-512.
15. Saliu A, Adebayo O, Kofoworola O, Babatunde O, Ismail A. Comparative assessment of blood lead levels of automobile technicians in organised and roadside garages in Lagos, Nigeria. J Environ Public Health. 2015; 2015.
16. Kassy CW, Uchegbu CK, Ango TJ. Symptoms Associated with Low Threshold Lead Poisoning Among Roadside and Organized Panel Beaters in Enugu

Metropolis, Nigeria. J Heal Pollut. 2021;11(29).

17. Dioka CE, Orisakwe OE, Adeniyi FAA, Meludu SC. Liver and renal function tests in artisans occupationally exposed to lead in mechanic village in Nnewi, Nigeria. Int J Environ Res Public Health. 2004;1(1):21-25.
18. Zhang L, Zhao CX, Ji HX, He J, Chang CF, Hao HY, *et al.* Effect of occupational lead exposure on the blood pressure of lead-exposed workers. Chinese J Ind Hyg Occup Dis. 2016 Nov 20;34(11):825-827.
19. de J. Bandeira M, dos Santos NR, Cardoso MS, Hlavinicka N, Anjos ALS, Wândega EL, *et al*. Assessment of potters' occupational exposure to lead and associated risk factors in Maragogipinho, Brazil: preliminary results. Int Arch Occup Environ Health. 2021;94(5):1061-1071.
20. Kuraeiad S, Kotepui M. Blood lead level and renal impairment among adults: A meta-analysis. Int J Environ Res Public Health. 2021;18(4174):1-33.
21. Adewale ALLI L, Adewale Alli L. Blood level of cadmium and lead in occupationally exposed persons in Gwagwalada, Abuja, Nigeria. 2015;
22. Orisakwe OE. Lead and Cadmium in Public Health in Nigeria: Physicians Neglect and Pitfall in Patient Management. N Am J Med Sci. 2014 Feb;6(2):61-70.
23. Goyal T, Mitra P, Singh P, Sharma S, Purohit P, Sharma P. Effect of occupational co-exposure to lead and cadmium on selected immunomodulatory cytokines. Toxicol Ind Health. 2022;38(1):1-10.
24. Zhou R, Xu Y, Shen J, Han L, Chen X, Feng X, et al. Urinary KIM-1: a novel biomarker for evaluation of occupational exposure to lead. Sci Rep [Internet]. 2016 [cited 2019 Sep 25];6:38930. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27966578
25. Assadi N. Is a Long Term Work in Automotive Industry a Risk Factor for Renal Dysfunction? Ann Med Health Sci Res. 2015; 5(2):103-107.11
26. Yu YL, Thijs L, Wei DM, Melgarejo JD, Yu CG, Yang WY, *et al.* Two-Year Responses of Renal Function to First Occupational Lead Exposure. Kidney Int reports. 2022; 7(6): 1198-1209.
27. Egwurugwu JN, Nwafor A, Oluronfemi OJ, Iwuji SC, Alagwu EA. Impact of Prolonged Exposure to Oil and Gas Flares on Human Renal Functions. Int Res J Med Sci. 2013;1(11):9-16.
28. Tsai HJ, Hung CH, Wang CW, Tu HP, Li CH, Tsai CC, et al. Associations among Heavy Metals and Proteinuria and Chronic Kidney Disease. Diagnostics (Basel). 2021;11(2):282-294.
29. Chukwukasi KW, Chikee AE, Ndudi OE, Nwabueze AE. Association between Lead Exposure and Haematological Parameters among Roadside and Organized Panel Beaters in Enugu Metropolis, Nigeria. J Occup Heal Epidemiol [Internet]. 2021 Jan 1 [cited 2022 Jun 21];10(1):48-56. Available from: http://johe.rums.ac.ir/article-1-421-en.html
30. Hsieh NH, Chung SH, Chen SC, Chen WY, Cheng YH, Lin YJ, et al. Anemia risk in relation to lead exposure in lead-related manufacturing. BMC Public Health. 2017 May 5;17(1).
31. Basit S, Karim N, Munshi AB. Occupational lead toxicity in battery workers. Pakistan J Med Sci. 2015;31(4):775-780.
32. Froom P, Kristal-Boneh E, Benbassat J, Ashkanazi R, Ribak J. Lead exposure in battery-factory workers is not associated with anemia. J Occup Environ Med. 1999; 41(2):120-123.
33. Steenland K, Barry V, Anttila A, Sallmén M, McElvenny D, Todd AC, *et al*. A cohort mortality study of lead-exposed workers in the USA, Finland and the UK. Occup Environ Med. 2017;74(11):785-791.
34. Madrigal JM, Ricardo AC, Persky V, Turyk M. Associations between blood cadmium concentration and kidney function in the U.S. population: Impact of sex, diabetes and hypertension. Environ Res. 2019 Feb 1;169:180-188.
35. Bernard A. Cadmium & its adverse effects on human health. Indian J Med Res. 2008;128(4):557-564.
36. Soderland P, Lovekar S, Weiner DE, Brooks DR, Kaufman JS. Chronic Kidney Disease Associated With Environmental Toxins and Exposures. Adv Chronic Kidney Dis. 17:254-264.