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Research Article

Kidney Function Status in Persons Occupationally Exposed to Heavy Metals in Metal Forging Factory in Nnewi, Southeastern Nigeria.

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ABSTRACT

Occupational exposure to heavy metals impacts negatively on human health especially on the functionality of the kidneys. This is a cross sectional study designed to assess the kidney function status in individuals who are occupationally exposed to heavy metals in metal forging factory in Nnewi. A total of 39 apparently healthy individuals in cable manufacturing factory workers aged between 19 and 56 years and 79 control subjects (comprising of 39 control subjects from Nnewi (N) and 40 control subjects from Elele (E) respectively) aged between 18 and 44 years were recruited for the study. 5ml of venous blood sample was collected from each subject for the determination of biochemical parameters (potassium, sodium, chloride, bicarbonate, urea and creatinine levels) using standard laboratory methods. Results revealed that there were significant elevations in the mean concentrations of plasma urea, creatinine, sodium and potassium ($p<0.05$) with a corresponding significant decrease in the mean plasma chloride and bicarbonate levels in the individuals occupationally exposed to heavy metals in metal forging factory ($p<0.05$), which suggest an impaired renal function in these individuals.

Keywords: *metal forging, heavy metals, kidney, kidney function, Length of service, Body mass index, Age*

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INTRODUCTION

Forging is the technology of shaping the metal piece into the desired shape. This technology is widely used in the industry for making well-defined and desired shape of metals. From using the simple hammer and anvil in the 12th century for making a simple shape to making the complex shape in present times, metal forging has witnessed various advancements in its ways (Bharti, 2017). Gaseous matters like gases, vapours, fumes and smoke and also particulates of heavy metals are produced during melting and pouring operations. The major pollutants are emitted from various work areas in Foundry i.e. Pattern shop, Sand preparation, moulding and core making, mould drying and ladle heating, cupola, electric arc furnace, pouring and mould cooling, knockout, fettling and heat treatment (Shrivastava, 2009).

Heavy metals are dangerous because they tend to bioaccumulate. Bioaccumulation means an increase in the concentration of a chemical in a biological organism over time, compared to the chemical's concentration in the environment. Compounds accumulate in living things any time they are taken up and stored faster than they are broken down (metabolized) or excreted (Joseph *et al*., 2010). Heavy metals become toxic when they are not metabolized by the body and accumulate in the soft tissues. Heavy metals may enter the human body through food, water, air, or absorption through the skin when they come in contact with humans in agriculture and in manufacturing, pharmaceutical, industrial, or residential settings. Industrial exposure accounts for a common route of contamination for adults. Ingestion is the most common route of exposure in children (Roberts, 1999).

It has been recognized that environmental toxins such as cadmium, lead, and arsenic play a significant role in the development of chronic renal failure. In addition, the combination of different metals has been shown to have a cumulative nephrotoxic effect (Ernesto and Ludivina, 2012). Environmental and occupational exposure to nephrotoxic substances may cause renal tubular and glomerular impairments (Marek, 2005). The kidney is particularly vulnerable to these effects because of its structure and function. The kidney receives one-fifth of the resting cardiac output, 10% of which undergoes filtration at the glomerulus. This brings large amounts of solutes/particulates to the glomerular and tubular compartments (Marek, 2005). Lead and most heavy metals absorbed in the body are mainly excreted through kidneys, and longstanding exposure to excessive lead concentrations may cause chronic nephrotoxic effects such as interstitial nephritis, tubular damage, and at later stages glomerular damage leading to the chronic renal failure (Sabath and Robles-Osorio, 2012; Soderland *et al*., 2010).

Observational studies have repeatedly reported an association between lead exposure and an increased risk of renal disease, but the intensity of exposure, which ultimately produces renal damage, is still a matter of debate (Ekong *et al*., 2006; Evans and Elinder, 2011). Up to the present, severe adverse effects of lead on the kidney have been reported mainly in subjects occupationally exposed in a working environment, which is the major source of heavy lead exposure (Ekong *et al*., 2006).

A study by Teresa *et al*. revealed measurable alterations of renal function in low-level lead exposure and suggests that glomerular hyperfiltration may be an early indicator of functional impairments in subjects occupationally exposed to lead (Teresa *et al*., 2015). Associations between increased GFR values estimated from creatinine clearance and higher lead exposure measures have been previously observed in subjects with long exposure histories and blood lead levels below 600 µg (Weaver *et al*., 2006). Previously the work of Amah *et al*. on the nephrotoxic effect of lead exposure among automobile repairers revealed high lead level with significant increases in the mean serum concentration of creatinine, urea, and uric acid in the automobile repairers than in the control subjects which may eventually lead to renal damage (Amah *et al*., 2014). Okpogba *et al*. also documented decreased bicarbonate level with no significant differences observed in the mean levels of potassium, sodium, chloride, urea and creatinine in the factory chickens in Nnewi (Okpogba *et al*., 2018). Further, Okpogba *et al*. had earlier recorded an elevated level of these heavy metals in Nnewi (Okpogba *et la*., 2019; Okpogba *et la*., 2019) which is the cardinal propelling force for the present study. Therefore, the current study assessed the renal function status in persons occupationally exposed to heavy metals in metal forging factory in Nnewi, Nigeria.

MATERIALS AND METHODS

Study design: This is a cross-sectional study designed to assess the renal function status in persons occupationally exposed to heavy metals in metal forging factory in Nnewi, Nigeria. A total of thirty-nine (39) apparently healthy individuals in the exposed group (metal forging factory workers) aged between 19 and 56 years were recruited for the study. The occupationally exposed group comprised workers from metal forging factory who were constantly being exposed to effluents from the factory. The control groups were made up of two (2) sets: The first set was made up of thirty-nine (39) staff and undergraduate students of the College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus whose residential homes were at least 5-10 km from the factory sites, while the second set was made up of forty (40) staff and undergraduate students of the Faculty of Medicine, Madonna University, Elele. They were aged between 18 and 44 years. Informed consent was obtained from all individuals after being educated on the benefit of the study and completing of a structured questionnaire. Thereafter, 5ml of venous blood sample was collected from each individual for the evaluation of biochemical parameters.

Estimation of Serum Creatinine Level: Serum creatinine level was assayed using Jaffe-Slot Alkaline Picric Acid Method as described by Laron (1972).

Estimation of Serum Urea: Estimation of serum urea level was done using Berthlot Method as described by Ochei and Kolhatkar (2007).

Determination of Electrolyte Profile Levels: Estimation of electrolyte (sodium, potassium, chloride and bicarbonate) profile levels was done using Ion Selective Electrode (ISE) Method.

Inclusion and exclusion criteria: Apparently healthy individuals aged between 19 and 56 years who are exposed to cable manufacturing factory effluents and control individual (non-exposed groups) were included in this study. Individuals of any known kidney disease, alcoholics and smokers as well as those outside the age limits were excluded from the study.

Ethical consideration: Ethical approval for this study was sought and obtained from Ethical Committee, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria (NAUTH/CS/66/Vol.2/149).

Statistical analysis:
The data were presented as mean±SEM and the mean values of the control and test group were compared by Students t-test and Pearson's bivariate correlation coefficient using Statistical package for social sciences (SPSS) (Version 16) software. A $P<0.05$ was considered as significant.

RESULTS

The urea concentration of control N subjects (5.32±0.09) was significantly elevated ($p<0.05$) compared with control E subjects (2.17±0.04) while the creatinine level of control N subjects (75.59±1.48) was higher than control E though non-significantly ($p>0.05$). The urea/creatinine ratio (U/C ratio) of control N subjects 70.70±32.57±0.86) was significantly elevated ($p<0.05$) compared to control E subjects (32.57±0.86), The results are shown in Table 1.

The sodium ion (Na^+) and potassium (4.14±0.19) level of metal forging (136. 06±1.58) factory workers were significantly elevated ($p<0.05$) compared to that of control N subjects (122.87±0.78). However, the Cl^- level of metal forging (84.11±7.26) factory workers were significantly reduced ($p<0.05$). Also, the bicarbonate ion (HCO_3^-) concentrations in the metal forging (22.50±2.07) factory workers were significantly reduced ($p<0.05$) compared to the control subjects (26.73±0.20).

The mean serum urea concentration of the metal forging (4.71±0.28) factory workers were reduced but not significantly ($p>0.05$) when compared to control N (5.32±0.09) subjects, however, they were significantly elevated ($p<0.05$) compared with control E (2.17±0.04) subjects. Creatinine concentration was significantly elevated ($p<0.05$) in metal forging factory workers compared with control group. The U/C ratio was significantly elevated ($p<0.05$) in metal forging factory workers compared with control E (32.57±0.86) subjects (See Table 1).

The effects of age of metal forging factory workers on the kidney function status is presented in Table 2, while the regression analyses are presented in Figure 1. Sodium ion was significantly elevated ($p<0.05$) in the age groups compared with the control subjects while K^+ was also elevated significantly ($p<0.05$) and Cl^- reduced significantly($p<0.05$) at the 41-50yrs age group. There was no significant difference ($p>0.05$) between the HCO_3^-, urea, creatinine and U/C ratio of factory age groups and the control except U/C ratio which was significantly elevated ($P<0.05$) in the 41-50yrs age group. Except for Cl^- (r=-0.287; p=0.247) which was negatively correlated, Na^+ (r=0.067; p=0.792), K^+ (r=0.446; p=0.063), HCO_3^- (r=0.033; p=0.896), urea (r=0.402; p=0.099), creatinine (r=.002; p=0.993) and U/C ratio (r=0.172; p=0.509) were positively correlated with age, though non-significantly ($p>0.05$) in each case.

Table 3 presents the effect of LOS on the kidney function status of metal forging factory workers while the results of the regression correlations are presented in Figure 2. There was no significant difference ($p>0.05$) between the LOS groups for Cl^-, HCO_3^- and creatinine levels and their respective control subjects, however, Na^+ levels were significantly elevated ($p<0.05$) compared to the control subjects. Urea levels of the factory workers was significantly reduced ($p<0.05$) in the 16.20 yrs LOS group while U/C ratio was significantly reduced ($p<0.05$) in the factory LOS groups compared to the control subjects. There was also no significant ($p>0.05$) correlation between all the kidney function parameters and LOS, however, Na^+ (r=0.066; p=0.794) , Cl^- (r=0.125; p=0.622) and U/C ratio (r=0.189; p=0.448) were positively correlated while K^+ (r=-0.155; p=0.551), HCO_3^- (r=-0.127; p=0.615), urea (r=-0.095; p=0.707) and creatinine (r=-0.245; p=0.328) were negatively correlated.

Table 1:
Kidney function status of metal forging factory workers and control group

Factory	Na^+ ion (mmol/L)	K^+ ion (mmol/L)	Cl^- ion (mmol/L)	HCO_3^- ion (mmol/L)	Urea (mmol/L)	Creatinine (μmol/L)	U/C Ratio
N (n=39)	*122.87±0.78^a*	*3.28±0.04^a*	*99.25±0.18^b*	*26.73±0.20^b*	*5.32±0.09^c*	*75.59±1.48^{bc}*	*70.70±0.66^b*
E (n=40)	*N/A*	*N/A*	*N/A*	*N/A*	*2.17±0.04^a*	*67.71±1.23^{ab}*	*32.57±0.86^a*
K (n=18)	*136.06±1.58^c*	*4.14±0.19^b*	*84.11±7.26^a*	*22.50±2.07^a*	*4.71±0.28^c*	*80.54±5.93^c*	*63.51±5.04^b*

Values are in mean (±SEM); within the column, mean with different superscripts are statistically significant (p<0.05).
***KEY**: **N**: Control subjects from Nnewi **E**: Control subjects from Elele **K**: Workers from metal forging factory*
***U/C ratio**: Urea/Creatinine ratio **N/A**: Not Analyzed*

Table 2:
Effect of age on kidney function status of metal forging factory workers

Age group	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)	HCO_3^- (mmol/L)	Urea (mmol/L)	Creatinine(μmol/L)	U/C ratio
N (n=39)	122.87±0.78^a	3.28±0.04^a	99.25±0.18^b	26.73±0.20^a	5.32±0.09^{ab}	75.59±1.48^a	70.70±0.66^a
18-30yrs (n=14)	135.93±1.86^b	4.14±0.23^{ab}	86.00±8.68^{ab}	21.43±2.45^a	4.43±0.31^a	82.72±7.51^a	58.89±5.55^a
31-40yrs (n=2)	132.50±5.50^b	4.05±0.65^{ab}	87.50±8.50^{ab}	29.00±2.00^a	5.34±0.85^{ab}	79.56±0.00^a	67.10±10.51^a
41-50yrs (n=2)	140.50±1.50^b	4.30±0.50^b	67.50±28.50^a	23.50±7.50^a	6.10±0.02^b	66.30±4.42^a	92.33±6.40^b

Values in mean (±SEM); Within column, means with different superscripts are statistically significant (p<0.05).
***KEY: N:** Control subjects **U/C ratio**: Urea/Creatinine ratio*

Table 3:
Effect of LOS on kidney function status of metal forging factory workers

LOS group	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)	HCO_3^- (mmol/L)	Urea (mmol/L)	Creatinine (µmol/L)	U/C Ratio
N (n=39)	122.87±0.78[a]	3.28±0.04[a]	99.25±0.18[ab]	26.73±0.20[a]	5.32±0.09[bc]	75.59±1.48[a]	70.70±0.66[b]
0-5yrs (n=12)	135.50±1.73[b]	4.15±0.21[b]	78.42±9.48[a]	23.17±2.65[a]	4.61±0.32[bc]	82.24±7.96[a]	60.62±6.16[a]
6-10yrs (n=2)	138.00±0.00[b]	5.30±0.60[c]	81.50±14.50[a]	21.50±9.50[a]	5.36±0.86[bc]	83.98±4.42[a]	63.39±6.80[a]
11-15yrs (n=2)	138.50±0.50[b]	3.35±0.45[a]	114.00±18.00[b]	21.50±9.50[a]	6.15±0.07[c]	79.56±8.84[a]	78.06±7.87[a]
15-20yrs (n=2)	135.00±13.00[b]	3.75±0.15[ab]	91.00±21.00[ab]	20.50±1.50[a]	3.25±0.26[a]	61.88±26.52[a]	66.46±32.64[a]

Values are in mean (±SEM); within column, means with different superscripts are statistically significant ($p<0.05$)
KEY: ***N:*** *Control subjects*
LOS*:* *Length of service*
U/C ratio: Urea/Creatinine ratio

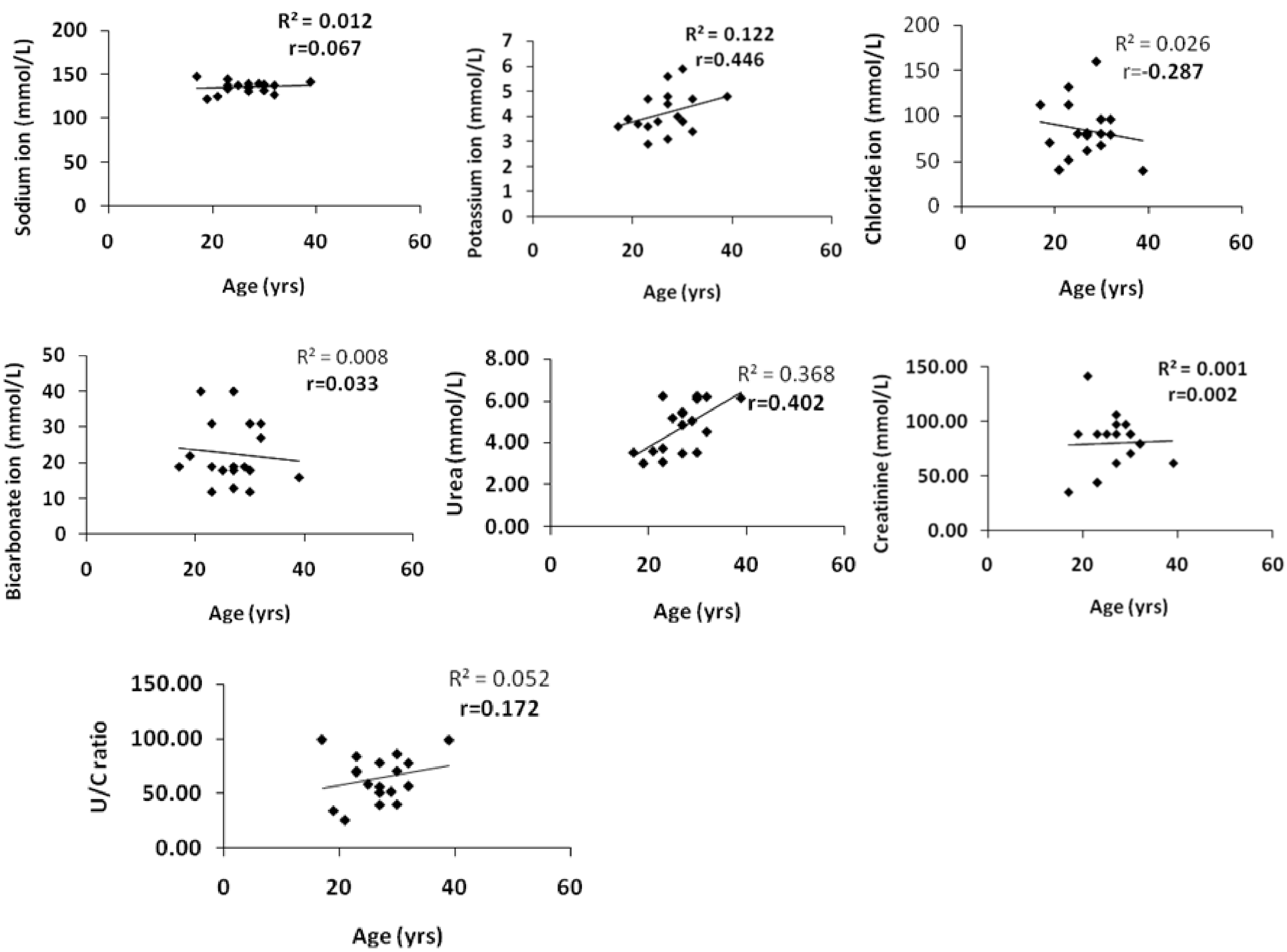

Figure 1:
Regression of kidney function status of metal forging factory workers with age

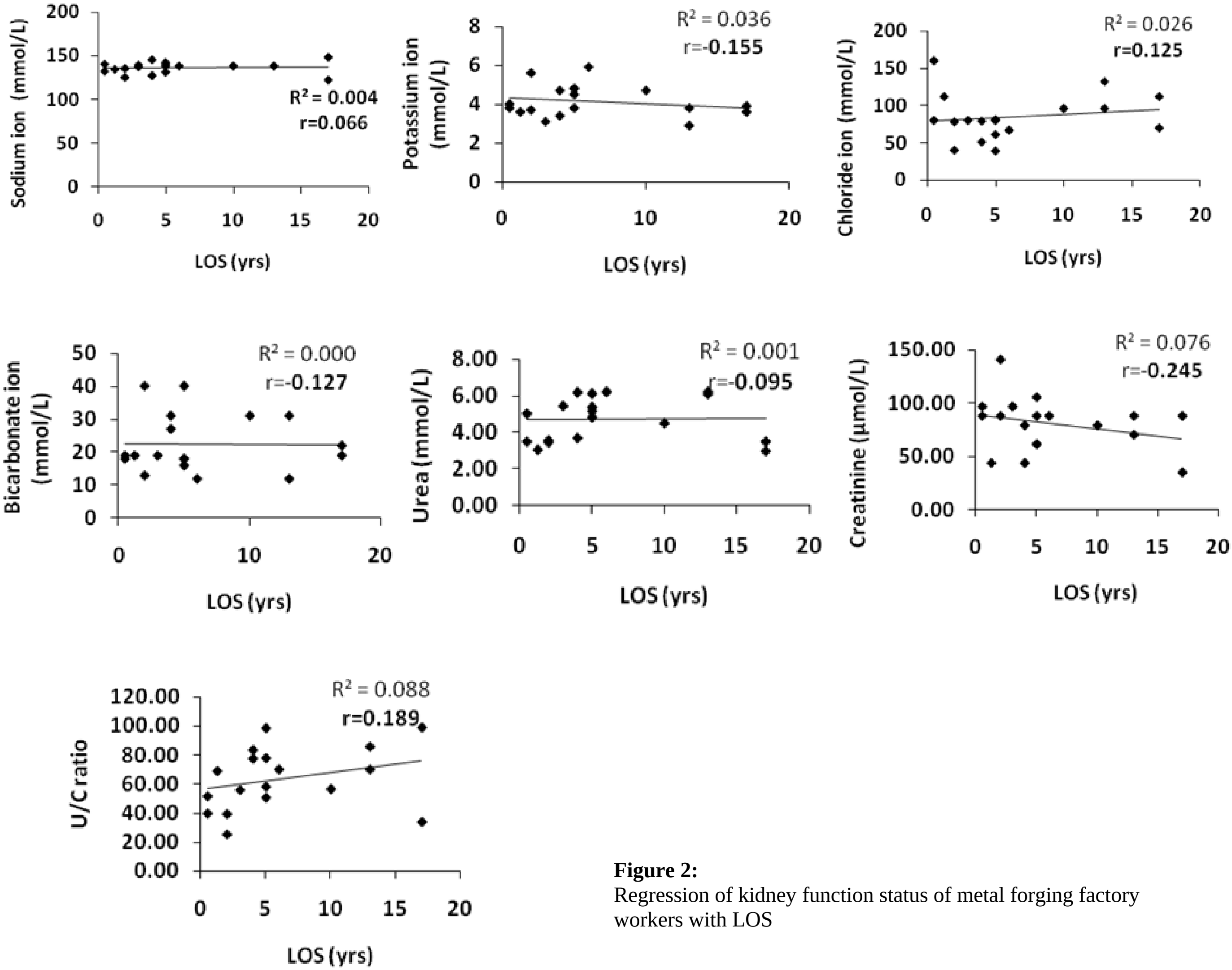

Figure 2:
Regression of kidney function status of metal forging factory workers with LOS

DISCUSSION

The exposure to heavy metals and environmental pollutants in metal forging factories which is constantly experienced by factory workers may impact negatively on their health especially with regards to the functional status of the kidneys as it is the principal organ majorly affected by these industrial pollutants. Heavy metals absorbed in the body are mainly excreted through the kidneys, and longstanding exposure to excessive heavy metal concentrations such as lead may cause chronic nephrotoxic effects such as interstitial nephritis, tubular damage, and at later stages glomerular damage leading to the chronic renal failure (Sabath and Robles-Osorio, 2012; Soderland *et al*., 2010). Thus, the present study assessed the renal function status in persons occupationally exposed to heavy metals in metal forging factory in Nnewi since elevated levels of heavy metals such as Ni, As and Pb has been reported earlier in the metal forging factory workers in this area (Okpogba *et al*., 2019).

In this study, the mean serum urea concentration of the metal forging factory workers was reduced but not significantly (p>0.05) when compared to control N subjects. This decrease in urea concentration in the metal forging factory workers may be due to the fact that these workers consume protein-deficient diet as urea production is a fall out of protein metabolism which increases with high protein intake. This is in consonance with the reports of some previous similar studies (Dioka *et al*., 2004; Orisakwe *et al*., 2007). However, the current urea concentration documented in this work is in contrast with the work of some other similar studies (Dongre *et al*., 2010; Amah *et al*., 2014) that showed elevated levels of urea in automobile factory workers. Furthermore, a significant increase in urea concentration was observed in the metal forging factory workers in this study when compared with the control E subjects (p<0.05) which is in keeping with the reports of similar studies (Dongre *et al*., 2010; Amah *et al*., 2014; Okpogba *et al*., 2018).

Creatinine concentration was significantly elevated (p<0.05) in metal forging factory workers compared with control group. This is in keeping with the findings of some previous documented studies (Dongre *et al*., 2010; Amah *et al*., 2014), but disagrees with the report of Zinat *et al*. who recorded a significant decrease in creatinine level in lead-exposed Bangladesh automobile workers (Zinat *et al*., 2012). Elevated levels of both urea and creatinine as observed in this study may be a pointer to the fact that the functionality of the kidneys in these metal forging factory workers are compromised. Both urea and creatinine are indicators of kidney function and are continually maintained within a reference limit in healthy subjects (Ahmed, 2011; Allen, 2012). Accumulation of these metabolites in the blood indicates renal disorder (Perazella and Khan, 2006; Appel *et al*., 2008). This finding corroborates the work of Amah *et al*., (2014).

Electrolyte panel is frequently used to screen for an electrolyte or acid-base imbalance and to monitor the effect of treatment on a known imbalance that is affecting bodily organ function. The test for electrolytes includes the measurement of sodium, potassium, chloride, and bicarbonate for both diagnosis and management of renal, endocrine, acid-base, water balance, and many other conditions. Potassium used as a most convincing electrolyte marker of renal failure. The combination of decreased filtration and decreased secretion of potassium in distal tubule during renal failure cause increased plasma potassium. Hyperkalemia is the most significant and life-threatening complication of renal failure (James and Mitchel, 2006).

The sodium ion (Na^+) and potassium (4.14±0.19) level of metal forging (136. 06±1.58) factory workers were significantly elevated ($p<0.05$) compared to that of control subjects (122.87±0.78). However, the Cl^- level of metal forging (84.11±7.26) factory workers were significantly reduced ($p<0.05$). Also, the bicarbonate ion (HCO_3^-) concentrations in the metal forging (22.50±2.07) factory workers were significantly reduced ($p<0.05$) compared to the control subjects (26.73±0.20). See table 1. This report agrees with that of Onuegbu *et al*. on the renal indices of people occupationally exposed to lead (Onuegbu *et al*., 2011). It, however, disagrees with the work of Babalola and Babajide (Babalola and Babajide, 2009), although they reported a significant increase in lead in a group of industrial workers in Ewekoro, Abeokuta granite industry, there was no difference in the sodium and potassium ions of the workers. The elevated sodium ion concentration observed in the serum of the factory workers obtained in this study may have arisen from water loss which is due to inappropriate regulation of osmolarity occasionally due to renal or hepatic disease or prolonged sweating without access to water. As for increased potassium ions observed in the metal forging factory workers, it may have been due to the inability of the kidneys to excrete ingested potassium probably due to dehydration (Leaf and Santos, 1961). Maintenance of the proper potassium ion concentration of the extracellular fluids is essential particularly for the proper functioning of the heart. High concentrations cause widespread intra-cardiac block while low concentrations impair the contractility of the heart muscle. Expectedly, sodium ion was significantly elevated in the age groups compared with the control subjects while K^+ was also elevated significantly ($p<0.05$) and Cl^- reduced significantly($p<0.05$) at the 41-50yrs age group. There was no significant difference ($p>0.05$) between the HCO_3^-, urea, creatinine and U/C ratio of factory age groups and the control except U/C ratio which was significantly elevated ($P<0.05$) in the 41-50yrs age group. Also, there were no significant correlations observed in the parameters studied.

Also, there was no significant difference ($p>0.05$) between the LOS groups for Cl^-, HCO_3^- and creatinine levels and their respective control subjects, however, Na^+ levels were significantly elevated ($p<0.05$) compared to the control subjects. Urea levels of the factory workers was significantly reduced ($p<0.05$) in the 16.20 yrs LOS group while U/C ratio was significantly reduced ($p<0.05$) in the factory LOS groups compared to the control subjects. There was also no significant ($p>0.05$) correlation between all the kidney function parameters and LOS.

In conclusion, this study has successfully shown that there were significant elevations in the mean concentrations of plasma urea, creatinine, sodium and potassium with a corresponding significant decrease in the mean chloride and bicarbonate levels in the individuals occupationally exposed to heavy metals in metal forging factory which suggest an impaired renal function in these individuals.

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