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Original Article

Impact of Occupational Exposure to Metallic Welding Fumes and Smoking on Reno-Hepatocellular Homeostasis in Relation to Serum Copper Level

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Abstract:

Background: Metallic welding is a highly skilled process that involves the joining of metals or metallic substances by heating to a specific temperature. Constant exposure to metallic fumes leads to organ and system injuries and deleterious health effects on welders. The study examined the effect of occupational exposure to metallic welding fumes and smoking on reno-hepatocellular homeostasis in relation to serum copper levels of welders.

Methods: Forty (40) subjects were recruited, comprising 10 welders who were smokers, 10 welder non-smokers, 10 non-welders that are smokers and 10 non-welders who were non-smokers. Blood samples were collected to estimate biochemical assays of liver and kidney parameters. The collected data were expressed in mean ± SEM, and a one-way ANOVA was used for comparison between means.

Results: Findings revealed a significant increase ($p<0.05$) in the levels of serum copper of welders compared with the control group. Urea levels were significantly increased ($p<0.05$) in welders who were smokers, whereas, levels of serum creatinine showed a non-significant decrease in welders who were smokers compared with the control group, and other experimental groups. For the liver function assays, the activities of Aspartate aminotransferase (AST) were not significantly different from those of the control. Activities of Alanine aminotransferase (ALT) were significantly increased ($p<0.05$) in non-welders that were smokers compared to those of the control. Remarkably, ALP activities were significantly decreased ($p<0.05$) in all experimental groups compared to control levels, the observed reduction was least in welders that are non-smokers. Total bilirubin and direct bilirubin levels were non-significantly increased. The level of total protein was significantly reduced ($p<0.05$) in smokers that were non-welders compared with the control group.

Conclusion: Exposure to fume particles from metallic welding, particularly copper, affected kidney function parameter values by significantly increasing urea levels and reducing creatinine levels in smoking welders. In summary, this study suggests that changes in serum copper levels among smoker welders may be associated with the severity of changes in kidney and liver functional status following exposure to metallic fumes with possible risk of hepatic dysfunction over time, especially when smoking is involved.

Keywords: *Metallic welding, Creatinine, Urea, Copper, Enzymes, Kidney, Liver, Smoking.*

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1. Introduction

The workplace is an important part of the human environment. Occupational exposure to hazards associated with metallic welding cannot be overstated, as workers are routinely exposed to toxic fumes linked to a wide range of severe acute and chronic health effects. As such, the overall health of workers in any organization is greatly affected by the conditions in their work environment, thus impacting their productivity, although, evidence suggests that no profession is without risk [1]. Exposure to metallic fumes is complex and varies significantly depending on the welding process, the electrode used and the material being welded. Obviously, metallic welding produces gases and small solid particles, collectively known as metallic fumes, most of this occurs in arc welding [1, 2]. Metallic welding processes generate hazardous substances like; gases, fumes, heat, noise, infrared radiation and ultraviolet which is very harmful to the eyes and deleterious to different organs of the body with risk of attenuating homeostatic processes [3, 4, 5]. Fumes from metallic welding are considered to be the most harmful compared to other welding by-products [6]. Particles contained in fumes from metallic welding are small enough to get airborne and are easily inhaled and potentially cause respiratory problems [1, 7].

Copper (Cu) is an essential trace element that becomes toxic at elevated concentrations. It is mainly used in agriculture as a pesticide and in the leather industry. Copper is required by the body most notably as a cofactor for a number of enzymes such as ceruloplasmin, cytochrome oxidase, dopamine ß-hydroxylase, superoxide dismutase and tyrosinase. Cu is present in different bodily tissues, and is primarily stored in the liver, but it is present in smaller amounts in the brain, heart, kidneys and muscles. Human exposure to copper occurs primarily through consumption of food and drinking water or fumes [8]. Occupational exposure to nephrotoxic metals like copper has been associated with tubular and glomerular injuries in welders. As a result of this exposure, welders develop an insidious incipient kidney and liver diseases related to the type of metal, electrodes and duration of exposure [9]. The health risk impact of metallic fumes depends to a large extent on the type of metal, the concentration of fumes, and the duration of exposure. The short-term effect could include; noticeable toxicity symptoms, allergies and irritation to the eyes, throat, nose and lungs, metal fume fever, and irritant-induced asthma, meanwhile, long-term health effects include; damage to the lungs, emphysema, pneumonia, bronchitis, and increased risk of respiratory cancers [10]. The kidneys and liver are not spared from the harmful effects of exposure to metallic fumes. Due to the compensatory ability of the kidneys, and detoxifying potentials of the liver, exposure to metallic fumes does not usually produce early clinical symptoms and becomes evident mainly during chronic exposure [5].

The kidney is a primary retroperitoneal bean shaped organ of the renal system located on the posterior abdominal wall outside of the abdominal cavity that play significant homeostatic role in the removal of metabolic waste products such as creatinine and urea out of the body [9, 11]. Creatinine is a waste product formed from creatinine phosphate. This conversion is spontaneous, non-enzymatic, and dependent on the body’s total muscle mass. It is not affected by diet, age or exercise. Serum creatinine levels have been used as a screen for renal function status. Urea is a parameter of kidney function also called carbamide (the diamide form of carbonic acid) which is a nitrogenous waste product from protein breakdown [9, 12]. Another major and very important secretory organ in the human body is the liver. It is a vital organ that makes up around 2% of an adult's body weight and is in charge of numerous processes including metabolism support, digestion, immunity, detoxification, and vitamin storage [13, 14, 15]. Since most fumes from metallic welding are initially stored largely in the liver when inhaled, prolonged exposure to metallic fumes causes pathobiological changes in the liver and other sensitive organs increasing oxidative stress and inflammation [16, 17, 18, 19]. Perhaps, exposure to toxic fumes from metallic welding can result in adverse health outcomes, including damage to the nervous system, liver and kidneys [15]. Some studies have suggested the effects of these fumes on liver is linked to complexity of the metallic fume compositions, variability in the levels of exposure, individual susceptibility levels, and the lack of robust long-term studies with large sample sizes, though the evidence in this area has conflicting results [20, 21, 22].

Smoking is the practice of inhaling smokes prepared from burning plant materials. Smoking negatively impact liver and kidney health by causing kidney damage, increasing the levels of blood urea and contributing to liver condition like; fatty acid disease, reduce blood flow, which is largely due to the contamination of the blood with components of tobacco smoke [23]. Not only can smoking increase the risk of kidney cancer, but it can also contribute to additional kidney damage. Smokers have a significantly higher risk of chronic kidney disease than non-smokers. A history of smoking promotes the progression of diabetic nephropathy. Outbreaks of certain types of diseases and infections have been found to affect smokers’ more than regular smokers. It is known that smoking tobacco, due to the toxic effects of the components, damages the liver and kidneys, causes cancer and the degeneration of kidney and liver cells. Smokers have a significantly increased risk of chronic kidney disease than non-smokers [22, 23]. Findings from previous study indicated that elevated blood urea levels above the normal range and higher creatinine and uric acid levels, suggest risk of hepatic dysfunction and buildup of potential renal diseases [24]. Chronic exposure to essential trace element and heavy metals like; lead, chromium, cadmium, and copper can induce an insidious but progressive tubular interstitial nephropathy that often leads to kidney failure [5, 24, 25]. Therefore, the study examined impact of serum metallic fumes on the functional status of the liver and kidney following exposure to smoking status as a modulator in welders.

2. Materials and Methods

2.1 Study design

The study adopted a cross-sectional analytical study design in collecting important information from among male smokers and non-smokers with a welding experience of more than one (1) year, who satisfactorily met the inclusion criteria. The participants were categorized into four groups as follows; Group 1 served as control; without history of welding job and who were non-smokers. Group 2 were smoker's that are non-welders, Group 3 were non-smokers welders, while Group 4 represents smokers who were welders.

2.2 Place of study

The area of study is Obiaruku and Abraka, with Obiaruku being the headquarters of the Ukwani LGA. It is one of the most important homelands of the Ukwani speaking people. It is made up of parishes and sub-districts, known as quarters, bordering Edo to the east, Abraka to the southwest, Eziopkor to the southeast, and Obinomba to the northeast. Abraka on the other hand shares a common border with Obiaruku, Abraka is at Ethiope East LGA with its headquarters as Isiokolo, it is home to 24 Urhobo Kingdoms, thus, study setting is popularly known as the university host community and has the main campus of the University.

2.3 Subjects

The study population comprised adult male welders residing in the Abraka (Ethiope East LGA) and Obiaruku (Ukwani LGA) communities. A total of 40 apparently healthy participants were recruited using a two-stage sampling technique. First, convenience sampling was utilized to identify and locate accessible welding workshops within the study areas. Subsequently, 20 consenting participants from each community were selected through simple random sampling by balloting without replacement. This randomization involved the use of 'Yes' and 'No' ballots, with only those selecting 'Yes' being enrolled in the final study cohort.

2.4 Exclusion and inclusion criteria

Only welders whose shops are located in Abraka and Obiaruku communities, respectively, and are within the ages of 18-64 years constituted the study participants. Only those who have worked at least for one year as welders and must have agreed to fill the informed consent form were recruited. The adults chosen seemed to be in good health and were not employed in the fields that dealt with aluminum or metallic fabrications. Individuals with neurological disorders, heart issues, fractures, arthritis, trauma, and hypertension were excluded from the study.

2.5 Ethical consideration

Ethical permission for this study was secured from the Research, Ethics and Grants Committee of the Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria (RBC/FBMC/DELSU /23/268). Prior to data collection, the proprietors of the welding workshops were contacted and duly informed about the study. In addition, each participant provided verbal informed consent after the study objectives and procedures had been clearly explained in their preferred language, including English, Pidgin, Urhobo, or Ukwuani.

2.6 Sample collection

Using a tourniquet, 5 mL sterile syringe and sterile needle, cotton wool, methylated spirit, 5 mL of venous whole blood samples were obtained from the study from each subject and were dispensed into labeled containers and transported to the laboratory for analysis. Samples were centrifuged using bucket centrifuge at 3000 rpm for 5 minutes. A micropipette was used to separate the plasma from the samples. The materials used for data collection include: syringe (for collecting venous blood), cotton wool for sterilization and stoppage of blood flow from the site of puncture, alcohol for sterilization of the site of puncture, tourniquet: a tool used to partially stop blood flow and make vein at site of puncture visible for easy blood collection. Hand gloves to protect the hands from infection while collecting data, sample containers used to store the blood collected for the experiment. Stadiometer was used for measuring the height of participants; bathroom weighing scale that is calibrated in kilogram for weight measurement; sphygmomanometer (a digital blood pressure monitor was used in measuring the blood pressure of both the systolic and diastolic), bucket centrifuge to spin samples collected for easy decanting and a refrigerator for preservation of blood samples collected.

2.7 Biochemical investigations

2.7.1 Serum copper assay:

Buck Scientific Analytical Methods for Atomic Absorption Spectroscopy (model 210/211 VGP) were used to examine the samples adopting the methods of Makino and Takahara, [26]. Dilution of the plasma was done with deionized water. The viscosity parameters of the diluted samples were approximated by performing the analysis against standards produced in glycerol. The concentration of each metal in each sample was shown on the digital readout after the metals were measured at a certain wavelength. The copper metal has a wavelength of 324.8nm and the metal was read using an acetylene gas to ignite the machine.

2.7.2 Serum creatinine assay:

Creatinine concentration directly relates to the amount of complex that forms. For this serum creatinine levels estimation, a randox test kit was utilized. A colorful complex is formed when creatinine and picric acid combine in an alkaline solution. Perform a new gain calibration in cuvette mode using fresh ddH2O. Select CREA from the run test screen and run water blank as described in the test manual. The reaction rate and absorption of the reaction product are very sensitive to temperature.

2.7.3 Serum urea assay:

For this serum creatinine levels estimation, a randox test kit was utilized.Ammonia and carbon dioxide are produced when urea is hydrolyzed in the presence of water and urease. In the presence of glutamate dehydrogenase, the ammonia produced in the first step mixes with α-oxoglutarate and NADH. Using new ddH2O, perform a new gain calibration in flow cell mode. From the perform Test screen, choose UREA, then follow the instructions to perform a water blank.

2.7.4 Alanine aminotransferase estimation:

For *alanine aminotransferase (ALT)* estimation, 0.5 mL of substrate was added into a test tube containing 0.5 mL of blood, the mixture is put in a water bath at 37^{o}c for 30 minutes, 0.5 ml of 2,4-dinitrophenylhydrazine was added to the solution and incubated for 20 mins. Then 5 mL of sodium hydroxide was added to mixture which turned brown and was placed in a spectrophotometer at 540 nm and results were obtained from the calibrated graph. Calculation = ALT (U/I) = change Abs/mm x 1750.

2.7.5 Aspartate aminotransferase estimation:

For *aspartate aminotransferase (AST)* estimation, 0.5 mL of the substrate, sodium azide was added to the test tube plus 0.5 mL of the blood or serum. It was then put in a water bath at 37^{o}c for 30 minutes. After this, 0.5 mL of 2, 4 dinitrophenylhydrazine was added to the mixture, incubated for 20 mins, and 5 ml of sodium hydroxide was added to the mixture which turned brown. It was then placed in a spectrophotometer at 540 nm and the results were read on the calibrated graph.

2.7.6 Alkaline phosphatase estimation:

For *alkaline phosphatase (ALP)* estimation, 1 mL of p-nitrophenyl phosphatase was added to 1 mL of the serum in a test tube, incubated for 30 mins and results were obtained from the spectrophotometer at 410 nm and correlated with values on the calibrated graph to give the results.

2.7.7 Bilirubin estimation:

The levels of bilirubin in the blood or urine are determined by a bilirubin test. A high bilirubin level may be a sign of biliary or liver illness. When making a differential diagnosis of hyperbilirubinemia, the estimation of total and direct bilirubin in the serum is crucial. Using a buck scientific atomic absorption spectrophotometer, model 210/211 variable giant pulse correction and biochemical assay test kits, blood serum was examined for total and direct bilirubin estimation levels.

2.7.8 Estimation of total protein:

The method developed by Fares, [27], was used to estimate the total protein level. The two main categories of total protein techniques are chemical and physical. The physical approaches include UV light absorption, refractive index, and specific gravity measurements. The majority of the chemical techniques are variations on the biuret reaction. The preferred technique for clinical laboratories is thought to be the biuret reaction.

2.8 Data analysis

Data collected were calculated using mean ± SEM. The one-way ANOVA statistics was used to compare means across groups. Tukey's HSD test was used for post hoc multiple comparison for association between variables. Graph Pad Prism version 8 was used to calculate the data. A $p<0.05$ was considered statistically significant.

3. Results

Figure 1 presents the levels of serum copper of welders following exposure to fumes and smoking. Data from our study showed that serum copper levels were significantly reduced (p<0.05) in non-smokers who were non-smoker welders compared to control group. The reduction in levels of serum copper in smokers' non-welders was not significant in comparison those of the control. In contrast, the serum copper levels were significantly increased (p<0.05) in smokers who were welders compared to smokers' non-welders and non-smokers welders. The observed increase was non-significant compared those of the control group.

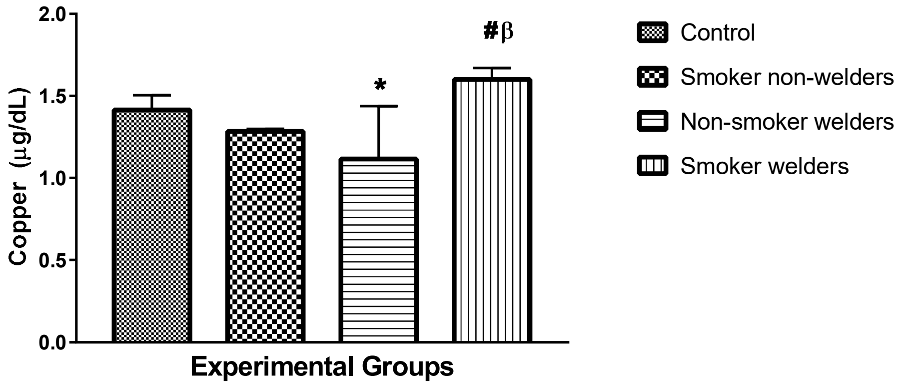

Figure 1: Levels of Serum Copper in Welders exposed to Metallic Fumes and smoking

**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared tosmoker welders*

The result from Figure 2 revealed that the levels of serum urea of welders were elevated following exposure to fumes and smoking. A graded increase in levels of serum urea in the various experimental groups compared those of the control was observed. However, a significant (p<0.05) increase in serum urea levels was only noted in smokers who were welders (smoker welders) compared to those of the control. In addition, non-significant difference was observed in serum urea level compared to the other experimental groups.

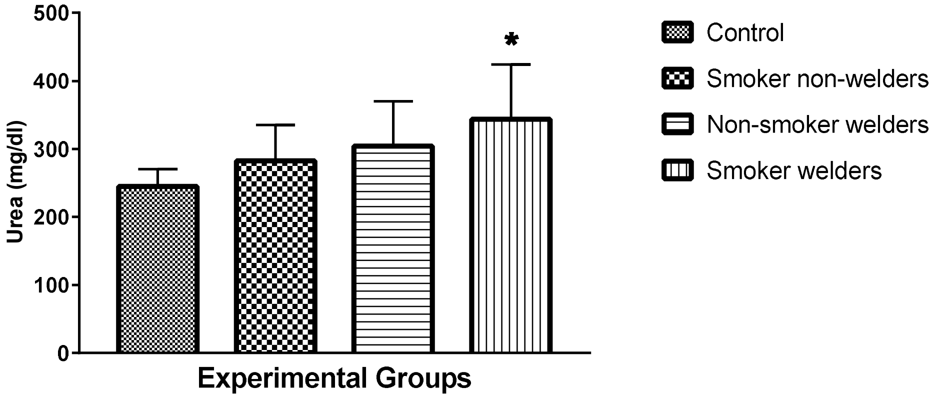

Figure 2: Levels of Serum Urea in Welders exposed to Metallic fumes and smoking

**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

The results presented in Figure 3 evaluated the serum creatinine levels of welders following exposure to fumes and smoking. The serum creatinine level across different experimental groups was not significantly different from those of the control. A significant (p<0.05) decrease was observed in the serum creatinine level in smokers who were welders (smoker welders) compared to welders who were non-smokers (non-smoker welders).

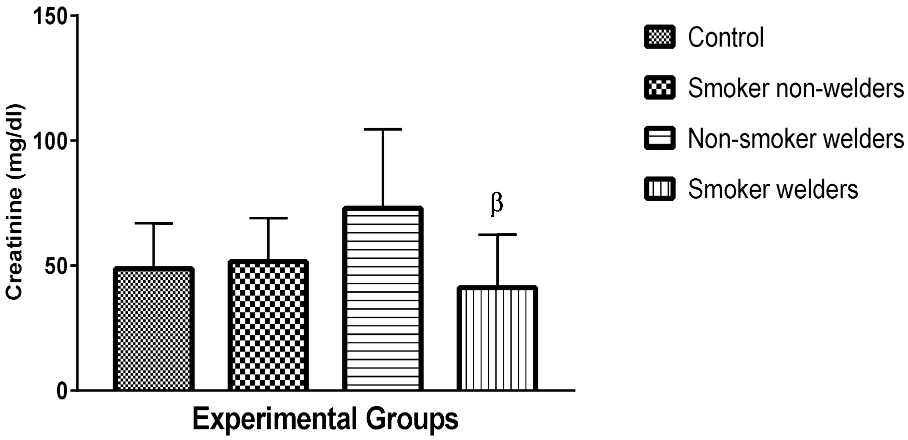

Figure 3: Levels of Serum Creatinine in welders exposed to Metallic fumes and smoking

**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

Results presented in Figure 4 evaluated aspartate aminotransferase (AST) activities in welders following exposure to fumes and smoking. Serum AST activities were elevated across all experimental groups and the noted increase were not significantly different compared to those of the control. The observed increase in the activities of serum AST was not significant across the experimental groups compared with the control group.

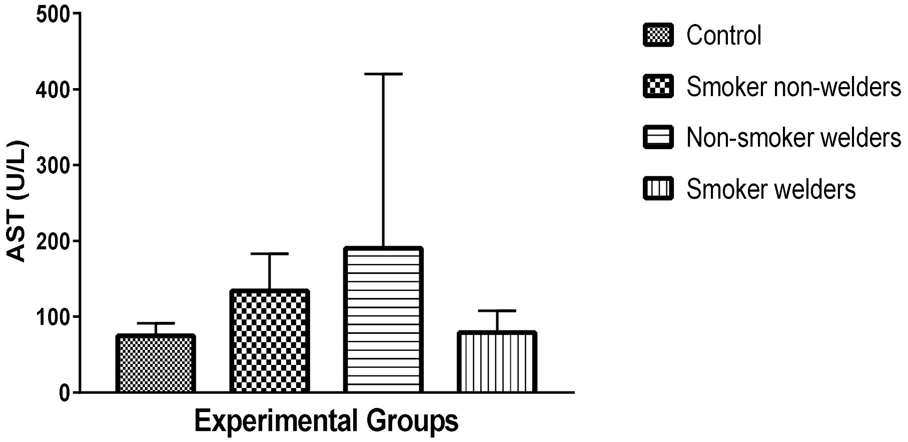

Figure 4: Aspartate aminotransferase (AST) activities in Welders exposed to Metallic fume and smoking

**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

Results presented in Figure 5 represent the activities of alanine aminotransferase (ALT) in welders following exposure to fumes and smoking. The present study revealed a significant ($p<0.05$) increased activities of serum ALT in smokers who were non-welders compared to control group. However, there was no significant difference noted in the activities of serum ALT when comparison was made between the different experimental groups.

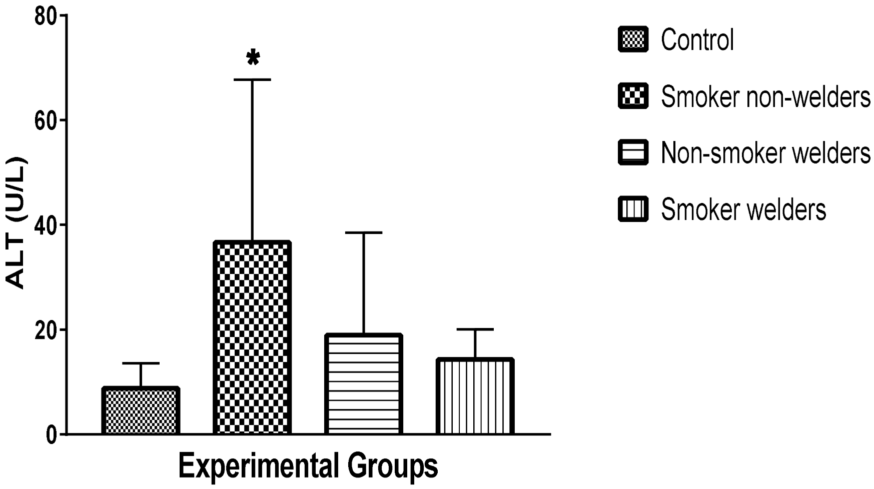

Figure 5: Alanine aminotransferase (ALT) activities in welders exposed to Metallic fume and smoking
**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

Result presented in Figure 6 illustrates the activities of alkaline phosphatase (ALP) in welders following exposure to fumes and smoking. This study recorded a significant (p<0.05) decreased activities of ALP across all experimental groups (smokers non-welders, non-smokers welders; and smokers welders), when compared to those of the control. The observed reduction in alkaline phosphatase (ALP) activities was least among welders who were non-smokers. However, there was no significant difference observed in the ALP activities when comparison was made between the different experimental groups.

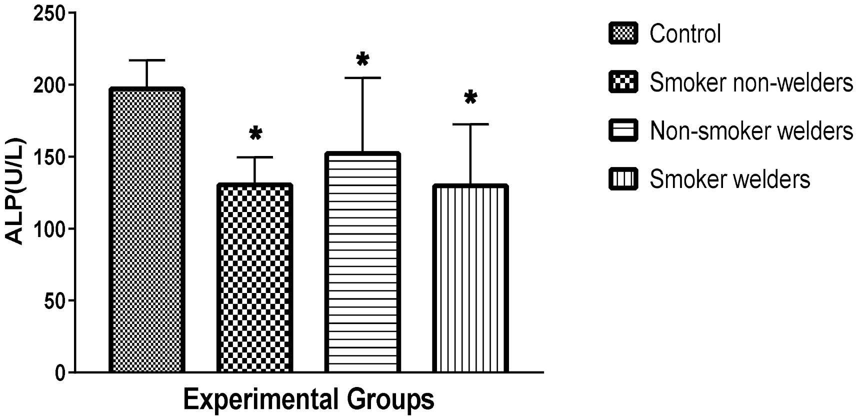

Figure 6: Alkaline Phosphatase (ALP) activities in welders exposed to Metallic fume and smoking
**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

Results presented in Figure 7, evaluated the levels of total bilirubin (a); direct bilirubin (b); and total protein (c) in welders following exposure to fumes and smoking. This study recorded a graded non-significant increased levels of total bilirubin across all experimental groups (smokers' non-welders, non-smokers welders and smoker welders), compared to control levels. Meanwhile, there was non-significant difference observed in the levels of total bilirubin when comparison was made between the different experimental groups. This study showed a non-significant increased level of direct bilirubin in smokers and non-smokers who were welders compared to those of the control group. However, a significant (p<0.05) increase in direct bilirubin level was observed among smokers who were welders (smoker welders) compared to smokers who were not welder (non-smoker welders). Similarly, the results revealed that total protein level of smoker non-welders was significantly (p<0.05) decreased compared to those of the control. However total protein levels of welders that are both smokers and non-smokers, was significantly (p<0.05) increased when compared to smoker non-welders.

(a) *(b)*

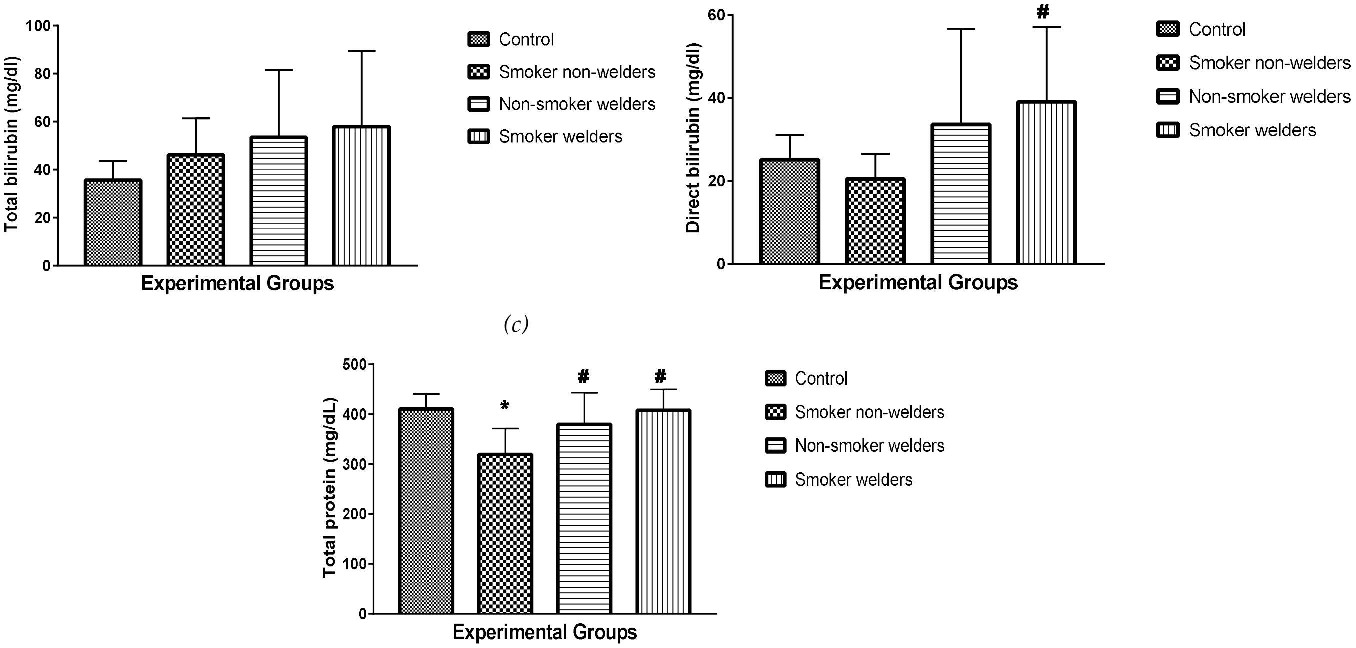

Figure 7[a-c]: Levels of Bilirubin (Total and Direct) and Total Protein in Welders exposed to Metallic fumes and smoking

**: Significant (p<0.05) compared to control; #: Significant (p<0.05) compared to smoker Non-welders, β: Significant (p<0.05) compared to non-smoker welders; +: Significant (p<0.05) compared to smoker welders*

4. Discussion

Fumes from metallic welding consist of a complex mixture of metal oxides, silicates and fluorides. Vapors are formed when a metal is heated above its boiling point and its vapors condense into very fine particles (solid particles). Metallic welding fumes generally contain particles from the electrode and the material being welded [22, 28]. The liver and the kidneys have the critical job of maintaining the body's metabolic homeostasis. This includes the processing of dietary amino acids, carbohydrates, lipids and vitamins: removal of microbes and toxins in splanchnic blood and route to the systemic circulation; synthesis of many plasma proteins; and detoxification and excretion into the bile of endogenous waste products and pollutants xenobiotics [29, 30]. The result in Figure 1 showed that the serum copper levels of welders exposed to metallic fumes. Serum copper levels of non-smoking welders were significantly reduced, why that of smokers were significantly increased compared to control, this is in line with that of El-Maksoud, et al. [31], who conducted a study on biochemical changes in occupational stress between smoking and non-smoking iron and steel workers in Egypt, this study found that exposure to metallic fumes is associated with high concentrations of Fe, Cu, Pb, Mn, MDA , catalase activity, cortisol and immunoglobulins and low activity of Zn, SOD, GR, GPX, GSH and NO. These can all be considered risk factors from exposure to metallic fumes in iron and steel workers [32, 33, 34, 35].

Data from our study showed that serum urea levels were significantly increased in the experimental groups, most significantly in smoking welders compared to those of the control (see Figure 2), this finding agreed with the opinion of Adejumo et al. [36] who conducted a study evaluating renal biomarkers of renal function in industrial auto workers in Benin City, Edo State, Nigeria, and they reported higher levels of some kidney biomarkers; urea and creatinine in autoworkers compared to controls. Specifically, they observed that blood urea levels were significantly elevated above the normal control range. Hence, their results suggest that occupationally exposed automotive workers may be at risk for kidney disease. Similarly, our finding is consistent with that of Duru, et al. [23], who conducted a study to assess the levels of serum cholesterol and urea in smokers and non-smokers, and found that serum total cholesterol levels and urea concentrations were higher in smokers than in non-smokers, suggesting that smokers are predisposed to cardiovascular disease and possible kidney problems [37].

Our results showed that the levels of serum creatinine of smoking welders was significantly decreased compared to non-smoking welders, and significantly increased in non-smoking welders compared to control (see Figure 3), such observe increase was similar with the view of Okpogba et al, [38], who conducted a study to assess renal function status in occupationally exposed individuals working in a metalworking factory in Nnewi, the study showed significantly increased levels of sodium, potassium, urea, and creatinine, and significantly decreased levels of both bicarbonate and of chloride ions due to exposure to heavy metals in the metal processing plant at

Nnewi. This suggests a possible association of exposure to heavy metals at the workplace on kidney function. A previous study examining the association between serum levels of cotinine and renal function in active and passive smokers, and found that kidney and glomerular functions can even be affected by secondhand smoke. In addition, an elevated microalbumin/creatinine ratio in these individuals may be a sign of an increased risk of atherosclerosis [39]. The observed reduction in serum creatinine levels in this study may have been influenced by factors beyond renal function.

Data from this study revealed increased activities of AST in non-smokers welders, followed by smokers' non-welders, smokers' welders and non-smokers and non-welders. The implication of this result is that the activities of AST in the serum of non-smokers, and non-welders were lower than welders that smoke and welders that don't smoke. Surprisingly, AST activity in serum of smokers' non-welder is higher than smokers' welders while it is lower than that of non-smokers welders. Although variations were observed, causal interpretation regarding smoking effects on AST was beyond the scope of this study. The increased activities of AST indicated possible risk of hepatic injury and this is explained by the leakage of enzymes from the tissue to the plasma due to the alteration of the membrane permeability [40]. Such observed increased activities of AST following exposure to metallic fumes among smoker welders is consistent with the views that many serum enzymes have are appropriate stress indicators [22]. Thus, activities of many serum enzymes, which included AST and ALT, have been frequently applied in the diagnosis of some of the cases of diseases, in addition, the discovery of impairment in tissues induced by environmental pollution. Therefore, the increased activity of the enzymes in the serum is considered a sensible indicator of minor cellular impairment subsequently tissue damage which results in stress [41, 42, 43].

The activity of ALT in serum of smokers who were non-welder was higher, followed by non-smokers welders, smokers' who were welders and the least activity of ALT were observed in non-smokers who were non-welders. The observed increase in the serum ALT activities of welders in this study could be attributed to alteration in the cellular membrane of the liver. The toxic materials in smokes caused an increase in cell membrane permeability leading to enzyme leaching or leakage of enzymes from liver to blood or another case the permeability has reduced which directly lead to the accumulation of enzymes in the hepatocytes which may increase the risk of hepatic dysfunction over time [44, 45]. Generally, the increase in activities of AST and ALT may infer deterioration changes and dysfunction of liver because the effect of toxicants on the hepatocytes induced in necrosis of the liver and thus, lead to leakage of these cellular enzymes into blood circulation. This is supported by the study of Rahimikia [46], who indicated that releasing these transaminases into the bloodstream which attribute to impairment of the hepatic tissue, heart, and kidney under stress affected by metal. In addition, he recommended that serum enzymes could be used in biomarkers to environmental toxicity. Thereby, these enzymes activity in serum is mostly resulted from inhaling from metallic fumes component of the cytoplasm of liver cells into the blood circulation due to liver damage via copper metal ions. The current research is in agreement with the finding by Naveed et al. [47] that frequent exposure to heavy metals led to increased activities of both aminotransferases, indicating enhanced transamination reactions.

Activities of ALP in serum of welders exposed to metallic fumes revealed that there was increased serum ALP activities in smokers who were non-welder compared those of the control and other experimental groups. The implication is that such increase observed in the activities of ALP may be due to the contents of what is being inhaled, not necessarily the metallic fumes alone. Previous research has demonstrated that smoking raises serum ALP activities produced by the kidney, liver, and bones [48, 49, 50]. Our results support the claims made by certain researchers that smoking increases ALP activities, other studies maintained that smoking and exposure to heavy metals had no effect on ALP [51, 52]. As a result, smoking's effects on ALP level may be complex due to a variety of extrahepatic pathways, as this study's findings did not consistently link smoking to levels of serum copper in welders exposed to welding smoke.

A graded increase (non-significant) in the serum total bilirubin level of all experiment groups was observed compared with the control group as illustrated in Figure 7[a-c]. Furthermore, a significant increase in direct bilirubin level was observed among smokers who were welders when compared to non-smokers who were non-welder. It can be deduced from this that the increase is as a result of the combined effects of smoking and metallic fumes. Meanwhile, in this study total protein levels was significantly decreased among smokers who were not welders. Metallic fumes significantly increased levels of total protein in welders (for both smokers and non-smokers) compared to non-welders who were smokers. However, the increase observed was not up those of the control. This result is in agreement with the findings of previous study reported that metallic welding process caused elevation in serum total protein, whereby, the rate of smoking is inversely related to an increased levels of total protein in participants [53].

5. Conclusion

Exposure to fume particles from metallic welding, particularly copper, affected kidney function parameter values by significantly increasing urea levels and reducing creatinine levels in smoking welders. The activities of AST, ALT and ALP varied significantly; such changes can be useful as a pointer of understanding the impact of elevated copper induced by metallic fumes on liver function of welders. Total and direct bilirubin levels revealed a graded non-significant increase, while total protein levels were decreased in relation to exposure to metallic fumes as exacerbated by smoking among welders. Interestingly, exposure to metallic fumes worsens reno-hepatocellular homeostatic status in smokers compared to non-smokers. However, no correlations were established between serum copper levels and renal function parameters, and no causal effect was observed. The elevated serum copper in the exposed groups does not exclude that other metals or substances that were not assessed could be the cause of these effects, hence, the need for further study.

Declarations

Consent for publication: All data generated or analyzed during this study are included in this published article.

Consent to Participate: An informed consent was obtained from all subjects and/or their legal guardian(s) prior to the study.

Data availability statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request. Due to privacy and ethical restrictions, the data are not publicly available.

Competing Interests: There is no conflict of interest to this study.

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Authors' Contributions: NBC and NOJ-F conceptualized and designed the study and participated in manuscript drafting. ESJ and EEI coordinated data collection and preliminary statistical analysis. NNT and OOB contributed to biochemical analysis and data validation. EMT and OMI provided supervisory oversight and timely manuscript revisions. OPO participated in literature search. All authors approved the final version of the manuscript.

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