Toxicology Reports 12 (2024) 48–55

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Modulatory role of welding fumes on serum zinc and copper levels and oxidative stress markers among welders: Considering smoking as a possible implication

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ARTICLE INFO

Handling editor: Prof. L.H. Lash

Keywords:
Welding Fumes
Antioxidants
Zinc
Copper
Welders
Smokers

ABSTRACT

The presence of heavy metals in welding fumes and the numerous metals that make up welding gases expose welders to numerous occupational dangers, including major occupational health issues worldwide. The gases from welding are a significant and highly skilled process that have a considerable negative impact on welders' overall health and wellbeing. This study evaluated the influence of welding fumes on serum zinc and copper levels and oxidative stress biomarkers in welders considering smoking as a potential risk factor. The study used a case-control experimental design. Forty (40) healthy adult males were randomly selected comprising twenty (20) in the experimental group involving smokers and nonsmokers with welding experience and twenty (20) in the control group involving smokers and nonsmokers without welding experience. Data are expressed as the mean ±SEM, and comparisons of means across groups were performed using one-way ANOVA, followed by Turkey's multiple comparisons test. The results showed that the serum zinc and copper levels of smokers were significantly ($p < 0.05$) increased in comparison to the control group, and a graded increase in the serum GST and MDA levels was observed across groups. The serum SOD level of smoker nonwelders was significantly ($p < 0.05$) increased when compared with the control group. Smokers who did not weld had significantly ($p < 0.05$) higher serum SOD levels. The results likewise showed a statistically nonsignificant reduction in glutathione levels and a substantial decrease in total antioxidant capacity (TAC) in the experimental group. Overall, changes in the antioxidant parameters showed that smoking and welding fumes can exacerbate an increase in the activity of reactive oxygen species (ROS), resulting in deteriorated health conditions.

1. Introduction

Millions of people are exposed to the dangers of welding each year. Different welding techniques have been identified for usage in industry [1]. A special environment for evaluating nanoparticle exposure and dose response in relation to oxidative stress generation in humans is provided by occupational settings such as welding. In industrial processes that involve joining metals by melting and fusing them through operations such as grinding, brazing, and soldering, welding is highly prevalent and crucial [2]. Among the various types, electric arc welding is considered the most common, in which heat fusion (temperature above 4000°c) is generated when electricity is passed through a gas between two electrical conductors [1]. Depending on the welding point, welders are exposed to welding fumes [3]. The welding process may expose workers to physical dangers, ergonomic stress, and chemical toxins, among other potential health risks. The impact of welding-associated air pollution on workers' health is one of these health risks that occupational medicine and public health consider to be of utmost importance [2].

Welding fumes, according to Sriram *et al.* [4] are complex and variable mixtures of gases and particles of various sizes. Sailabaht *et al.* [5] maintained that welding fumes are created when metals are heated over their melting point, evaporate, and condense into fumes. Very small particles make up welding fumes, which are mostly produced by

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https://doi.org/10.1016/j.toxrep.2023.12.007
Received 6 October 2023; Received in revised form 30 November 2023; Accepted 19 December 2023
Available online 21 December 2023

consumables such as fluxes, wires, and rods [6]. As a consequence of the welding process, welding fumes have a certain composition and rate of formation depending on the type of material being welded and the soldering equipment being utilized [2]. According to AnuarIthnin *et al.* [3] welding gases have relatively tiny particle sizes. Riccelli *et al.* [1] asserted that welding fumes contain metal oxide particles such as aluminum (Al), cadmium (Cd), cobalt (Cr), copper (Cu), fluoride, iron (Fe), lead (Pb), manganese (Mn), magnesium, molybdenum, nickel (Ni), silica, titanium, and zinc (Zn). According to the research by Riccelli *et al.* [1], welding fumes from some metals contain a complex mixture of toxic fumes and noxious gases, including ozone (O^3), nitrogen oxide (NOx), carbon dioxide, carbon monoxide, hydroxyl radicals (·OH), superoxide anion (O_2^-), H_2O_2 and singlet oxygen (1 O_2), which may cause ROS that have detrimental effects on human health [7].

Zinc is a crucial trace element involved in numerous metabolic processes as a catalyst, structural component, and regulatory ion [8]. It contributes to cell division, protein DNA synthesis, wound healing, and immunological function. Additionally, zinc aids in growth and development and maintains healthy senses of taste and smell. Zinc has antioxidant and antimicrobial properties and offers protection against premature aging [9]. Chemically, copper is an element with the symbol Cu and atomic number 29. It is a ductile metal that is soft, malleable, and has a high thermal and electrical conductivity. Pure copper surfaces that have recently been exposed are rosy-orange. In addition to its use as a building material, copper is also used as a component of several metal alloys, including cupronickel, which is used to make coins and marine accessories, and constantan, which is used to make strain gauges and thermocouples for temperature measurement [10]. The cupric ion (Cu^{2+}), the most significant oxidative state of copper (Cu), is a transition metal that is abundantly dispersed in nature. The brain and liver have the largest quantities of it, while it is present in all cells and organs [11].

Cigarette smoke, in addition to being poisonous, cancer-causing, and mutagenic substances, also contains stable and erratic free radicals, ROS in the particle and gas phases, and the potential for biological oxidative damage [12]. Smoke from cigarettes is a complex mixture of several substances that have the potential to cause cancer and other harmful effects, as well as stable free radicals, ROS, and gaseous free radical species. These chemical species, particularly the stable semiquinone radicals in tar, can interact with the biopolymers in the smoker's lungs. Welders who smoke had a greater rate of faulty pulmonary function tests, which is overwhelming evidence for the crucial role ROS and free radicals play in cigarette smoke poisoning [13]. Hydroxyl radicals produced by tar in aqueous tobacco can cause oxidative DNA damage [14].

Oxidative stress occurs as a result of an imbalance between the antioxidant enzymes of stabilizing agents, which are capable of quickly detoxifying reactive intermediates, and the systemic expression of reactive oxygen species [15,16]. A vast range of potentially harmful chemicals are exposed to welders. Preliminary evidence has shown that welding fumes can produce free radical activity, and welding fume particles, especially metallic particles such as zinc and copper, have garnered attention because they can elicit oxidative stress responses [17]. Most of these metals accumulate in the body throughout the course of a person's lifetime after prolonged exposure, which disrupts their normal serum levels and has biological effects that shorten the natural longevity of vital organs in the body such as the kidneys, liver, heart, brain and lungs, and can ultimately lead to their early failure [18]. It becomes imperative to carry out a study to evaluate the health effect of welding fumes on serum copper and zinc levels and some oxidative stress markers, specifically; glutathione, SOD, MDA and TAC markers among welders considering the likelihood of smoking as a possible implication.

2. Materials and methods

2.1. Materials used

The following materials and instruments will be used in the study: methylated spirit, cotton wool, 5 ml syringe and needle, blood test tubes, hand gloves, sterile bottles, plain sample containers, and study questionnaire. In addition, chemicals for estimating oxidative markers.

2.2. Experimental design

The effects of welding fumes were assessed in smokers and nonsmokers with more than a year of welding experience using a case-control experimental protocol as the research design. The study participants were carefully selected using a random sampling technique. All welding shops operating in Abraka, Ethiope East Local Government Area of Delta State were visited and blood samples were duly collected for biochemical investigations.

2.3. Participants

A total of forty (40) participants were recruited and used for the study out of a target population of 250 smoking and nonsmoking welders in the study area. The sample size was calculated using the Taro Yamane sample size determination formula of 1967. The formula is $n = N/(1 + N(e)2)$; where n = sample size, N = research population size, and e= precision level at 5% (0.05).

2.4. Selection criteria

Welders in continuous employment for 5–20 years. Welders aged 18 years and above. Smoking and nonsmoking welders were recruited. Individuals whose occupation is not related to welding or welding fume exposure and whose residential area is not close to any welding shops.

2.5. Experimental grouping

The experimental grouping of participants for the study was based on welders and nonwelders as well as smokers and nonsmokers as presented in Table 1 below:

2.6. Ethical approval

The Research, Ethics and Grants Committee of the Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria, was obtained prior to this study. The permit number: RBC/FBMC/DELSU/23/268 was obtained. The heads of each welding shop were consulted, and verbal consent was gained from each participant after a detailed discussion in their preferred language (English, Pidgin, Urhobo, or Ukwuani).

2.7. Blood sample collection

Using a tourniquet, cotton wool, methylated spirit, a 5 ml syringe,

Table 1
Experimental grouping.

Category	Description (n = 10)
Group 1	Negative control group comprising of individuals who are nonsmokers and are nonwelders or whose residential area is not close to any welding shop
Group 2	Positive control group comprising of individuals who are smokers but are nonwelders or whose residential area is not close to any welding shop
Group 3	Experimental group comprising of individuals who are nonsmokers but are welders who have exposure to welding fumes
Group 4	Experimental group comprising of individuals who are smokers and are welders who have exposure to welding fumes

and a sterile needle, whole blood was drawn from the cubital vein via venipuncture. The laboratory biochemical examination for zinc and copper levels and oxidative markers were evaluated using plasma decanted from the blood samples.

2.8. Biochemical examination

2.8.1. Serum zinc and copper estimation

The samples were read on a Buck Scientific Atomic Absorption Spectrophotometer model 210/211 VGP. The metals were read at a desired wavelength and the concentration of the metal in each sample was displayed on the digital readout. Each metal has its own wavelength, and a lamp, and the metals were read using acetylene gas to ignite the machine.

2.8.2. Reduced glutathione (GSH) estimation

The varied tissue homogenates were tested for reduced glutathione levels using the Ellman, [19] colorimetric method which is based on the reaction of GSH with 5,5′-dithiobis (2-nitrobenzoic acid) (DTNB). In 1 ml of 0.2 M Tris EDTA buffer, 100 ml of water was added, and the mixture was then incubated at 250 °C for 15 min. To obtain the precipitate, it was centrifuged. To produce a relatively stable yellow color, 5,5 dithiobis-2-nitrobenzoic acid (DNTB) was added, followed by incubation at 370 °C for 15 min. The absorbance at 412 nm was read against a blank containing 3.5 ml of buffer using a spectrophotometer, and the equivalent GSH content was calculated using the standard GSH curve provided in the kit.

2.8.3. MDA estimation

The method of Olaniyan *et al.* [20] was used to estimate the amount of malondialdehyde (MDA). MDA is more frequently used as a measure of ROS and lipid peroxidation. Thiobarbituric acid (TBA) was added to microcentrifuge tubes containing serum samples before they were incubated. After incubation, the samples were centrifuged for 10 min at a speed of 2000 rpm to measure the absorbance of the clear pink supernatant at 532 nm. Malondialdehydebis- (dimethylacetal) was employed as the external standard. The reactive compounds to thiobarbiturate were represented as nanomole MDA/gram of total protein. Thiobarbituric acid reactive substances (TBARS), which are formed during lipid peroxidation, were used to measure lipid peroxidation.

2.8.4. Total antioxidant capacity (TAC) estimation

The serum total antioxidant capacity was assessed using the methods of Benzie and Strain, [21]. By combining buffer acetate and TPTZ solution in HCl, FRAP (ferric reducing antioxidant power) was created as a functional solution. $FeCl_3$ was then introduced and combined. A total of 2400 liters of the aforementioned working solution and 80 liters of serum were combined and incubated at room temperature for 10 min. At 532 nm, the optical densities of the samples were measured.

2.8.5. Superoxide dismutase (SOD) activity estimation

The superoxide dismutase activity was determined by its ability to inhibit the auto oxidation of epinephrine determined by the increase in absorbance at 480 nm as described by Sun and Zigma, [22]. The reaction mixture (3 ml) contained 2.95 ml 0.05 M sodium carbonate buffer pH 10.2, 0.02 ml of liver homogenate, and 0.03 ml of 2 mM epinephrine in 0.005 N HCl will be used to initiate the reaction. The cuvette contained 2.95 ml buffer, 0.003 ml of substrate (epinephrine), and 0.02 ml of water. The absorbance was read at an interval of 1 min for 3 min at 480 nm.

2.9. Data analysis

The data collected were analyzed using the mean+SEM and one-way ANOVA. Turkey's multiple comparison test was used to test for post hoc associations between variables in GraphPad Prism, and version 8 was used to compute the data. A significant difference was considered when the p-value is < 0.05.

3. Results

The results from the present study, as shown in Fig. 1, represents the levels of serum zinc in workers exposed to welding fumes. Comparison of the levels of serum zinc among smoker nonwelders and nonsmoker welders with the control group revealed no significant difference. Similarly, no significant changes were observed in the levels of serum zinc when comparison was made between smoker nonwelders and nonsmoker welders. However, the levels of serum zinc were significantly ($p < 0.05$) increased in smoker welders when comparison was made with the control group and when compared with smoker nonwelders and nonsmoker welders respectively.

The results from Fig. 2 reveal the serum copper levels in workers exposed to welding fumes. There was a reduction in serum copper levels among smoker welders, and this reduction was not significant compared to the control serum copper levels. Serum copper levels were significantly ($p < 0.05$) decreased in non-smoker welders when compared with the control group. Conversely, the serum copper levels were significantly ($p < 0.05$) increased among smoker welders when compared with the levels of serum copper in smoker nonwelders and nonsmoker welders.

The results from the present study as illustrated in Fig. 3, evaluated the levels of serum glutathione in workers exposed to welding fumes. Serum GSH levels of smoker nonwelders, nonsmoker welders and smoker welders were reduced when compared with the control group. However, the observed decrease was not significant. Similarly, comparison of the serum GSH levels between the different experimental groups revealed no significant difference.

The results from Fig. 4 present the serum glutathione S-transferase (GST) levels in workers exposed to welding fumes. This study recorded a graded increase in the serum GST levels across the different experimental groups when compared with the control group. However, the observed increase in the serum GST levels was only significant ($p < 0.05$) in welders who were smokers when compared with the control group. More so, comparison of the serum GST levels between the different experimental groups revealed no significant difference.

Fig. 5 illustrates the levels of serum SOD activity in workers exposed to welding fumes. The results obtained revealed that the levels of serum SOD in smoker nonwelders was significantly increased ($p < 0.05$) when compared to the control group. The levels of serum SOD of nonsmoker welders were significantly ($p < 0.05$) decreased when compared to the serum SOD levels of smoker nonwelders. Furthermore, it was observed that the levels of serum SOD of smoker welders were elevated, however, this increase was not statistically significant when compared to the control levels, but was significant ($p < 0.05$) when compared to the nonsmoker welders.

Fig. 6 illustrates the levels of malondialdehyde in workers exposed to welding fumes. The results obtained revealed that the levels of MDA were nonsignificantly ($p > 0.05$) increased across all experimental groups when compared to the control group. However, no significant difference was observed in the levels of MDA when comparison was made between the different experimental groups.

The results from Fig. 7 represent the serum total antioxidant capacity (TAC) in workers exposed to welding fumes. This study recorded a significant decrease ($p < 0.05$) in serum TAC levels among smokers who were not welders (smoker nonwelders) when compared to the control levels. Meanwhile, the serum TAC levels of the nonsmoker welders and smoker welders were also slightly decreased; however, the noted reduction was not significantly different from the control levels.

4. Discussion

The system for handling and controlling the amount of key trace

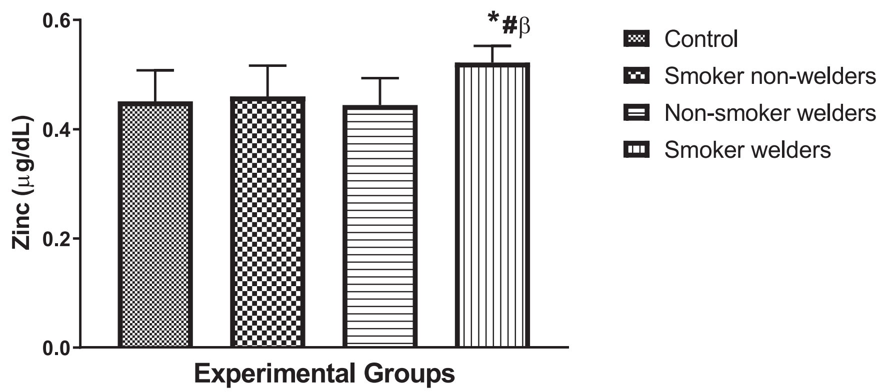

Fig. 1. Evaluation of serum zinc levels in welders exposed to welding fumes*: Significant in comparison with control #: Significant in comparison with smoker nonwelders β: Significant in comparison with nonsmoker welders.

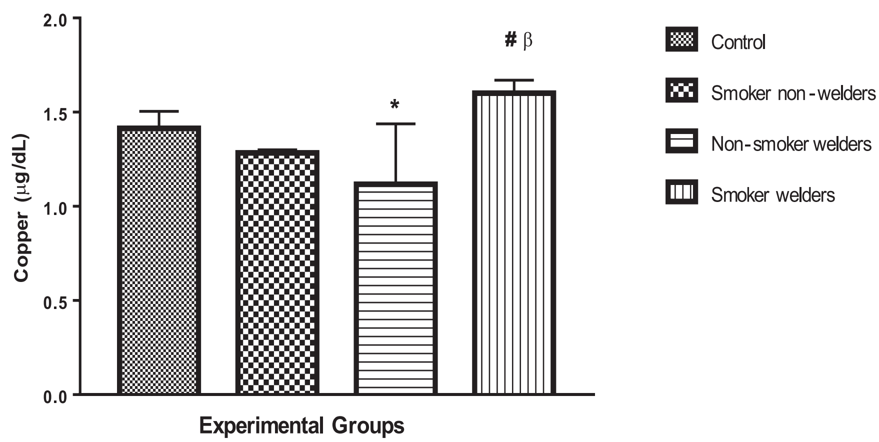

Fig. 2. Evaluation of serum copper levels in welders exposed to welding fumes*: Significant in comparison with control #: Significant in comparison with smoker nonwelders β: Significant in comparison with nonsmoker welders.

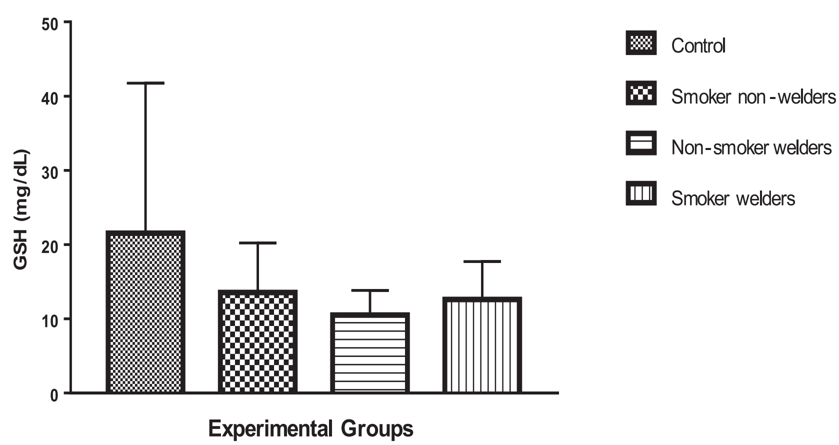

Fig. 3. Evaluation of Serum Glutathione levels of welders exposed to welding fumes *: Significant in comparison with control #: Significant in comparison with smoker nonwelders β: Significant in comparison with nonsmoker welders.

elements circulating in human blood and their storage in cells is exhaustive. The metals from our diet are assimilated into the blood, if blood levels are diminished, they are shifted into cells, if cellular levels are not enough, they are excreted if blood and cell levels are sufficient or overloaded. If the system cannot function in a proper manner, abnormal trace element ratios and concentrations might occur [23]. Examples of such commonest trace element disturbances are linked to serum copper and zinc concentrations present in welding fumes. Data from our study as represented in Fig. 1, revealed that the level of zinc was significantly ($p < 0.05$) increased in smoker welders when compared with the control zinc levels. It can be deduced from that welding fumes caused a significant increase in the zinc levels of the experimental subjects. This finding was consistent with that of previous study, who reported elevated serum zinc levels in metal fume fever [24], and another study who reported elevated lead, zinc, cadmium, copper, and chromium levels among occupationally exposed automotive workers [25]. However, our result

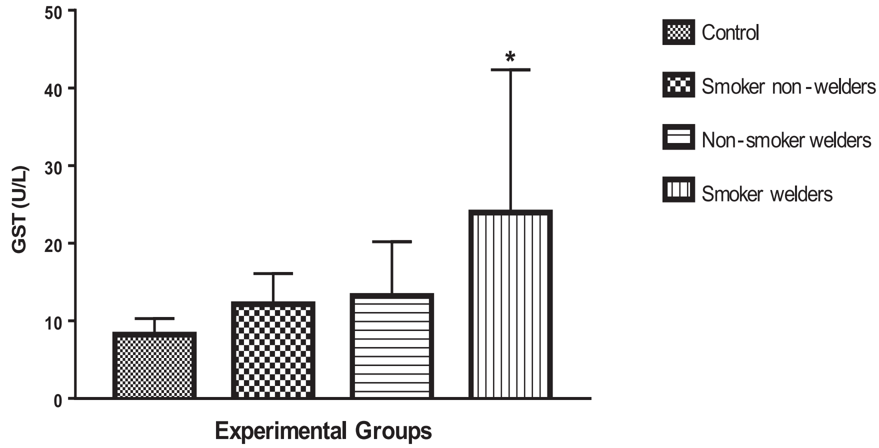

Fig. 4. Evaluation of Serum Glutathione S-transferase Levels in Welders exposed to Welding Fumes * : Significant in comparison with control #: Significant in comparison with smoker nonweldersβ: Significant in comparison with nonsmoker welders.

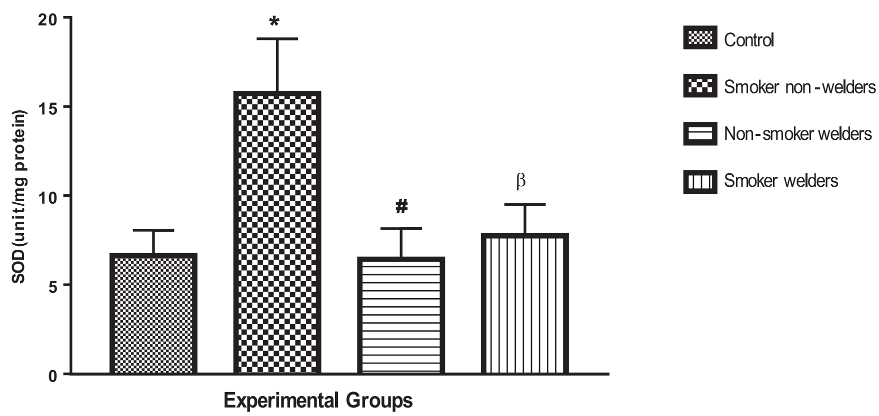

Fig. 5. Serum superoxide dismutase levels in workers exposed to welding fumes *: Significant in comparison with control #: Significant in comparison with smoker nonwelders β: Significant in comparison with nonsmoker welders.

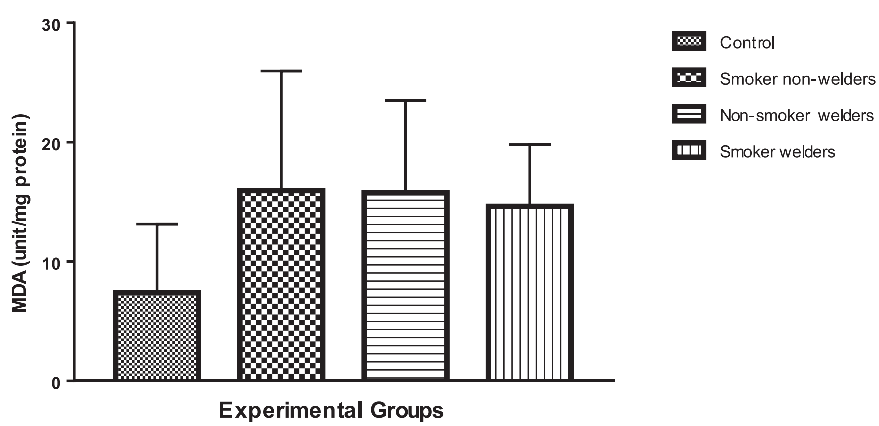

Fig. 6. Serum malondialdehyde levels in workers exposed to welding fumes *: Significant in comparison with control #: Significant in comparison with smoker nonweldersβ: Significant in comparison with nonsmoker welders.

contradicts the findings of Abdullahi and Sani, [26], who reported no significant changes in the zinc levels in welders. The contrary findings may be due to the composition of the welding fumes and the materials being welded.

As illustrated in Fig. 2, serum copper levels among nonsmoker welders were significantly ($p < 0.05$) decreased when compared to the control levels. This was in contrast to Adejumo *et al.* [25] findings, which showed a rise in serum copper levels in welders. In contrast, in our study welders who were smokers had significantly higher serum copper levels than nonsmokers and nonsmokers, respectively ($p < 0.05$). Welders who smoke as found in a previous study had significantly higher mean serum levels of copper, lead, cadmium, manganese, iron, and chromium compared to the control group [27]. The increase in copper levels can be attributed to welders' exposure to smoking in addition to welding fumes. Royer and Sharman, [28] affirmed that elevated serum copper levels indicate exposure to excess copper or may be linked to conditions that

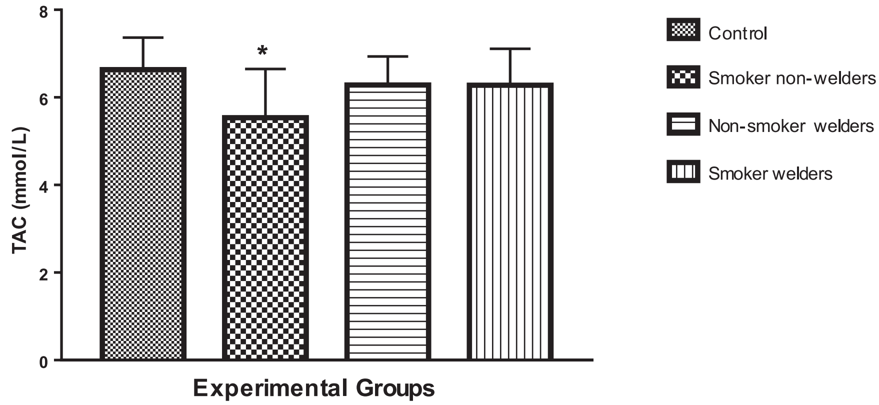

Fig. 7. Serum total antioxidant capacity (TAC) levels in welders exposed to welding fumes *: Significant in comparison with control #: Significant in comparison with smoker nonweldersβ: Significant in comparison with nonsmoker welders.

decrease copper excretion/ metabolism, such as; chronic liver disease, or that release copper from tissues, such as acute hepatitis.

A significant antioxidant and redox regulator in cells is glutathione. It serves as cofactor for numerous enzymes in addition to playing crucial roles in redox homeostasis [29]. According to the current investigation, as shown in Fig. 3, serum GSH levels in the experimental groups were not substantially lower than those in the control group or between experimental groups. This outcome is consistent with those of Han *et al.* [30] and Fatma *et al.* [31], who reported that serum glutathione levels had decreased. By binding electrophiles that would otherwise bind to proteins or nucleic acids and cause cell damage and gene mutations in a reduced form, glutathione conjugation aids in detoxification. GSH is a common intracellular peptide with various functions including detoxification, antioxidant defense, maintenance of thiol state, and regulation of cell proliferation [32]. Chronic exposure to metal fumes has been reported by Gad (2014) to influence the body oxidant-antioxidant status of the body and decrease its capacity for oxidative defense mechanisms when the oxidative stress chain begins in the body.

Glutathione-S-transferase is a phase II detoxifying enzyme and ubiquitous scavenger that functions by catalyzing the conjugation of GSH via cysteine thiols with a different nature of xenobiotic to reduce oxidative stress impact [33]; thus, GST is a biomarker for detecting stress, monitoring pollutants and exposure to environmental toxicants such as metal fumes [29,34]. As such, higher exposure to welding fumes triggers an increase in total GST activity. Our study recorded an increase in serum GST activity across the different experimental groups in comparison to the control group (see Fig. 4). However, this increase was significant in welders who were smokers when compared with the control serum GST activity. Such an increase in GST activity especially among smoker welders observed in this study agrees with the opinion of Gwarzo and Ujah, [35], who maintained that GST activity may have helped to limit the creation of MDA as a result of the agents' metabolism in the fumes, which may have helped to produce ROS. However, the mechanism by which cigarette smoking exacerbates the level of exposure to welding fumes is unknown.

Almost all living cells that are exposed to oxygen include an antioxidant defense enzyme known as superoxide dismutase [36,37]. According to the results of the current investigation, the blood SOD levels of smokers' nonwelders were substantially higher ($p < 0.05$) than the control levels and those of nonsmokers. Our results are consistent with those of Sung *et al.* [38], who found that welders had significantly higher levels of the antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD) than did participants who had not been subjected to welding. Smokers may have enhanced SOD activity as a result of potential oxidative stress caused by increased ROS generation. It is possible that prolonged smoking triggers oxidative stress, leading to an increase in these antioxidant enzymes, especially among welders who smoke. Such increased oxidative stress might stimulate the formation of more antioxidant enzymes to compensate for the consumed SOD and other antioxidant enzymes. Additionally, we discovered that nonsmoker welders' serum SOD levels were considerably (p 0.05) lower than those of nonsmokers who did not weld. This is in line with the findings of Salem, [27] who discovered that welders had a significantly lower mean value of blood total superoxide dismutase than the control group.

Malondialdehyde (MDA) levels were found to be increased in all experimental groups in comparison with the control group, according to the findings shown in Fig. 6. A higher MDA level denotes more lipid peroxidation. Our results are consistent with a study by Sattarahmady *et al.* [39], which found that welder individuals had higher MDA levels (nmol/ml) than control subjects. The activation of lipid peroxidation (MDA) increases under heavy metal stress, and an increasing amount of MDA represents the formation of free radicals under heavy metal stress [40,41]. This could explain the reported difference in the range of MDA activity found in our study. The level of MDA in smoking welders was increased nonsignificantly in comparison with the control group. This outcome was consistent with other research that showed that tobacco smoke includes a significant amount of free radicals that can cause or promote oxidative damage. According to Salem, [27] smoking increases the concentration of serum MDA activity and increases lipid peroxidation products in the blood compared to nonsmokers.

Fig. 7 shows that serum TAC levels in smoker nonwelders was statistically significantly lower ($p < 0.05$) when compared to the control levels. An improved in-vivo antioxidant defense status and increased TAC level are indicators of antioxidant absorption. This suggests that smoking negatively impacted serum TAC levels in both nonwelders and welder smokers. This result agrees with that of Hu *et al.* [42], who found that the TAC level among welders was lower than that of the control group. Reduced TAC levels indicate diminished or compromised antioxidant defense, tipping the scales in favor of oxidants. Our results were in agreement with existing research, who found that smokers who weld had considerably lower plasma antioxidant capacity than nonsmokers [27]. This could imply that smokers' lower plasma antioxidant capacity may be caused by a severe sulfhydryl depletion in plasma proteins.

In all, this study was limited by difficulty encountered in eliciting information on extent of exposure to welding fumes, possibility of quantifying the fumes been exposed to, as well as difficulty in the collection of blood sample from the respective participants, however, data were collected prospectively based on years of job experience in welding. In addition, the analysis was not designed to prove whether or how welding fumes might directly cause oxidative stress rather how occupational exposure to welding fumes could interfere with homeostasis of trace elements such as; zinc and copper in systemic circulation thereby inducing oxidative stress among welders considering smoking as possible implication.

5. Conclusion

It has been observed that welding fumes increase serum levels of copper and zinc trace elements connected to oxidative stress. According to our findings, exposure to welding fumes increased serum GST activity, and the levels of SOD and MDA. Lowering serum GSH and TAC levels in welders, particularly in smokers, also caused oxidative stress. All things considered, changes in antioxidant markers show that smoking and welding fumes can exacerbate an increase in ROS activity, which can lead to compromised health conditions. Since smoking may have an impact, quantitative studies of oxidative stress markers in the serum of welders may be useful in observing changes brought on by exposure to welding fumes. However, since few studies have been reported in this area, future researches are required for proper confirmation.

CRediT authorship contribution statement

NBC conceptualized, reviewed and edited the manuscript; **OMI** was involved in data curation and drafting of methodology; **UEU** was in-charge of project administration and supervision; **BD** conducted biochemical investigation; **ENJ** searched for literatures.All authors approved the submission of the manuscript for publication.

Declaration of Competing Interest

There is no conflict of interest.

Data availability

Data will be made available on request.

Acknowledgements

Not Applicable.

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