Toxicology Reports 8 (2021) 422–428

Contents lists available at ScienceDirect

Toxicology Reports

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

Histopathological changes associated with exposure to metal welding fumes in some organs of *Rattus norvegicus* in Kano, Nigeria

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ARTICLE INFO

Edited by Dr. A.M. Tsatsaka

Keywords:
Assessment
Histopathology
Organs
Welding fumes

ABSTRACT

Welding fumes has been known to cause release of reactive oxygen species which stands to be cytotoxic. The study aims to assess the histopathological changes of some organs associated with exposure to welding fumes in experimental animals. The metal fumes were obtained from sites of welding. A total of 130 male albino rats were engaged and divided into a 13 groups. Out of which 12 were given respective doses calculated to be equivalent to worker's real life exposure times and 1 as control. The doses were intratracheally administered weekly following anesthetization for a period of 12 weeks. The laboratory rats were then sacrificed and target organs were examined. Histopathological examination reveals normal feature for brain tissues in all treated animals. However, there was lymphocyte hyperplasia and necrosis in heart, kidney, liver and lungs tissues which at lower doses were slight and became moderate at higher doses. In addition, there were'nt pathological changes in tissues of the control animals. Thus, exposure to metal welding fumes has caused damages that have translated into lesions and several pathologies in kidney, lungs, liver and heart tissues of the test animals. Regulation and control should be imposed on exposure to welding fumes by metal workers.

1. Introduction

Metal works or welding is one of the major and widespread economic activities in Nigeria. In Kano, in particular, metal works have dotted the urban states landscape and been one of the major economic activities in the area. In a single settlement street, there can be about 2–3 units of shops for metal works with at least 5–10 people in a single unit. Usually, most houses, business buildings and other institutions use metallic products as sheets, pipes or rods [1]. The toxic effects from exposure to metal welding fumes and particulates are largely overlooked. The extent of the problem in the population of Nigeria is not at present known.

Workers could be exposed to metals related to welding via ingestion or skin contact. This is important in risk assessment of welders as during the process of ingestion/drinking of food/any liquid and a high level can be taken in. These pathways (ingestion/drinking) become important because lung cancer has been related with food containing large amounts of arsenic and chromium. Moreover, many metals which include beryllium, chromium and cobalt could cause irritation or allergy to the skin or could be absorbed via the skin and results in lung damage and some other health problems. Skin absorption is enhanced by small particle size and by cuts or other damage to the skin. The distribution of fumes in facilities was determined through surface wipe sampling [2]. The effects on respiratory parts included chronic and acute bronchitis, airway irritation, chemical pneumonitis, asthma related to occupation, and probable elevation in lung cancer as stated by [3]. Some research have been undertaken to evaluate the toxicity of welding fumes using both in vitro and in vivo models. It was described that fumes of stainless steel associated with manual metal arc welding induced higher cytotoxicity on rat macrophages than from fumes generated from other processes of welding [4,5]. Antonini et al. [6,7] demonstrated similar observations with a release of reactive oxygen species (ROS).

Welding fumes has significantly affected the blood indices (RBC, WBC and PLT) [8] and blood levels of metals in *Rattus norvegicus* [9]. Similarly, toxicity signs were observed in rats exposed to welding fumes and significant [9]. The chemical compositions of the fumes were found to affect its toxicity more than the size [10].

What organ(s) are the most susceptible to the metal fumes? What concentration of the metal fumes could bring damage to human tissue/

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https://doi.org/10.1016/j.toxrep.2021.02.016
Received 17 January 2020; Received in revised form 8 February 2021; Accepted 20 February 2021
Available online 25 February 2021

organ? Such answers are not only important but necessary in order to broaden the scope of environmental health issues in urban Kano.

2. Materials and methods

2.1. Collection of metal welding fumes

The metal fumes used in the study were produced in a fume cubicle with an open front chamber having a capacity (volume = 1 m^3). It was performed by a well skilled welder performing manual metal welding (shielded manual metal arc welding) process that utilized a stainless steel hard surfacing electrode and the fumes were subsequently collected on a 0.2-μm nuclepore filters. They were collected in significant amount at a welding site in Kofar Ruwa, Kano just before the start of the study. Only a single sample was collected over a period of 1 h and determined to be less than 1 μm by scanning electron microscope as stated in a previous study of the authors [9]. Moreover, the fumes sample were suspended in distilled water and then sonicated for 1 min. The total sample suspension was incubated for 24 h at 37 °C. The suspensions of the sample was digested and then subjected to analysis by Atomic Absorption Spectrophotometer as described by [9].

2.2. Experimental design

Male *Rattus norvegicus* (Albino rats) were chosen for this study. They were kept at the Animal house section of Department of Pharmacology in Aminu Kano Teaching Hospital, Kano, Nigeria. Randomized block design was used in this study. 130 albino rats were incorporated in the study. They were kept to acclimatize for fourteen (14) days before treatment and weigh about 210–250 g. The animals were divided into 13 experimental groups with each group composing of 10 albino rats allocated randomly to the groups [9,11].

2.3. Housing conditions

The animal house was free of pathogens and other extraneous factors with restricted access. The rats were kept in cages and marked respectively for identification. The animal room's temperature was maintained at about 22 °C (±3 °C) and humidity of at least 30 %. With respect to lightning, the pattern was 12 h light and 12 h dark. They were fed with a conventional laboratory diet and water *ad libitum*. There was adherence with the existing protocols for the use of lab animals strictly and ethical clearance for the study was obtained from Research Committee on Ethics, College of Health Sciences (CHS-REC) in Bayero University, Kano [12].

2.4. Preparation of test substance

The study involved sub-chronic toxicity testing of the metal fumes in albino rats which lasted for 12 weeks and the treatment was administered to the animals weekly by instillation intratracheally as described by Antonini et al. [13]. The doses used in the present study were depicting the real exposures of metal workers at workplaces in Kano. A mathematical simulation was used to evaluate the daily lung burden of a metal worker over a specified number of hours work schedule [14,15]. Below are the endpoints and factors that were taken into account during the calculation:

- Fume concentration (5 mg m^{-3}, threshold limit value for welding fumes) [16]
- Human minute ventilation volume (20,000 ml min^{-1} × 10^{-6} m^3 ml^{-1})
- Exposure duration (no. of hr day^{-1} × 60 min h^{-1})
- Deposition efficiency (15 %) [17,18].

With respect to the above factors, metal workers daily burden for various hours per day

1 Metal worker daily burden (2 h/day) = Fume concentration (5 mg/m^3) × Human minute ventilation volume (20,000 mL/min × 10−6 m^3/mL) × Exposure duration (2 h/day × 60 min/hr) × Deposition efficiency (15 %) =1.8 mg:

Using surface area of alveolar epithelium (rat = 0.4 m^2; human = 102 m^2) as dose metric [19]. Rat daily burden of exposure was taken as 0.0070mg

Then, similar exposure in rats for 3yrs, 5yrs, 10yrs and 20yrs will be 7.66 mg, 12.77 mg, 25.55 mg and 51.10 mg respectively at 365 days per year. Each of these concentrations was then divided into 12 which was administered weekly for the period of the study (12 weeks)

2 Metal worker daily burden (4 h/day), As in above, same exposure in rats for same years as in above would be 15.44, 25.73, 51.46 and 102.93 mg taking 365 days per year.

3 Metal worker daily burden (8 h/day), As in above, same exposure in rats for same years as in above would be 30.88, 51.46, 102.93 and 205.86 mg taking 365 days per year.

The Table 1 below represents the dosage of metal fumes administered on rats for 12 weeks. Each dose was given to a rat per week [8].

2.5. Administration and dose of test materials

Sterile saline was used to prepare the sample of the metal fumes and subsequently sonicated for 1 min to make the fumes dispersed. The rats were anaesthesized with ketamine (0.1 mL/100 g b.w IP) and then followed by the instillation of the dose intratracheally to the animal once in a week for a period of 12 weeks. However, 200 μl of sterile saline was administered to the control animals through intratracheal route after been equally anaesthesized. The process of intratracheal instillation was a commonly utilized technique to administer welding particulates into the lungs of laboratory animals. In such respect, welding fume is collected onto the filters, later suspended in an aqueous medium, and administered directly into the lungs of animals. Significance of such procedure over the inhalation technique includes simplicity, relatively low cost, and most importantly, the administration of a well-defined dose of particles [20–22].

2.6. Inclusion and exclusion criteria

All live experimental rats after termination of the experiment were included while dead rats were excluded from further examination. All collected samples were treated.

2.7. Histophatological examination

The animals were anaesthetized using chloroform and sacrificed 1 week after the last 12 weekly treatments by cutting the jugular vein with a blade. Surgical knife was used to remove target organs [23]. Histological processing: Formal-saline-fixed Lungs, liver, kidney, heart and

Table 1
Doses of metal fumes administered on rats every week for 12 weeks.

Groups		
I	II	III
Group IA (0.64 mg/animal/week)	Group IIA (1.29 mg/animal/week)	Group IIIA (2.57 mg/animal/week)
Group IB (1.06 mg/animal/week)	Group IIB (2.14 mg/animal/week)	Group IIIB (4.27 mg/animal/week)
Group IC (2.13 mg/animal/week)	Group IIC (4.29 mg/animal/week)	Group IIIC (8.56 mg/animal/week)
Group ID (4.26 mg/animal/week)	Group IID (8.58 mg/animal/week)	Group IIID (17.16 mg/animal/week)

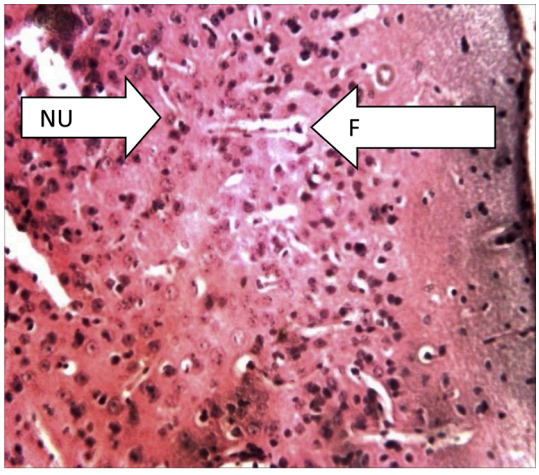
brain were dehydrated and embedded in paraffin wax. Thick sections of the tissues of about eight (8) μm were cut using a rotary microtome. They were subsequently stained by Hematoxylin and Eosin (H&E) method as stated by Bancroft & Cook [24]. The pictures were taken with a Leitz Light Microscope at magnification of ×250.

2.8. Precision and accuracy

The microscope has precise control of the specimen movement and focusing by the low position mechanical stage controls and Coaxial coarse and fine focus controls. It has excellent focus and concentration when changing objectives and comfortable viewing angle by the machined nosepiece and 45 degree viewing angle.

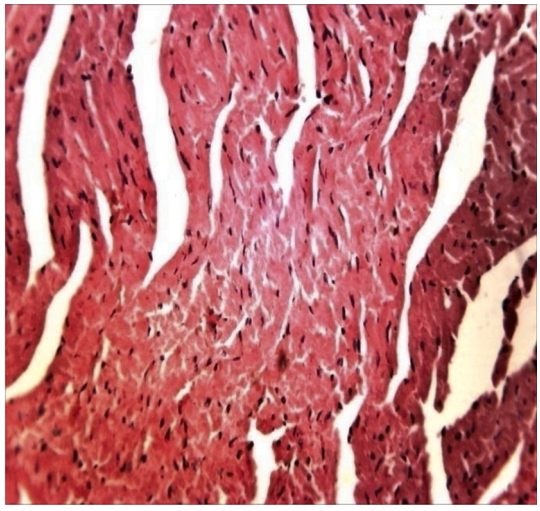
3. Results

The results of histopathological examination were shown in Fig. 1–5. Groups IA, IB, & IC showed no any change in the histological properties of brain, heart, kidney, liver and lungs. Similarly there were no changes in brain and heart tissue of group ID. However, there was slight lymphocyte hyperplasia in kidney and slight necrosis with lymphocyte hyperplasia for liver in group ID test animals. In lungs, there was observed moderate lymphocyte hyperplasia and alveoli congestion in lungs of group ID test animals as seen in Table 2. Groups IIA & IIB showed normal features in the histological properties of brain, heart, kidney, liver and lungs. Similarly there were no changes in brain and heart tissue of group IIC. However, there was slight lymphocyte hyperplasia in kidney and slight necrosis with lymphocyte hyperplasia for liver in group IIC test animals. Normal features for brain tissues were observed in group IID. Meanwhile, there was a slight necrosis in the heart and liver. In addition there was slight glomerular necrosis and lymphocyte hyperplasia in kidney. Similarly, there was alveolar congestion and moderate lymphocyte hyperplasia as observed in Table 3. In Table 4, there were no changes in brain and heart tissue of groups IIIA & IIIB. However, there was slight lymphocyte hyperplasia in kidney and slight necrosis with lymphocyte hyperplasia for liver in group IIIA & IIIB test animals. Normal features for brain tissues were observed in group IIIC. However, there was a slight necrosis in the heart and liver tissues. In addition there was slight glomerular necrosis and lymphocyte hyperplasia in kidney. Similarly, there was alveolar congestion and moderate lymphocyte hyperplasia. Normal features for brain tissues were observed in group IIID. However, there was a slight necrosis in the heart myocardium with moderate glomerular necrosis in kidney tissues and slight vascular congestion with vascular congestion in liver tissues. In addition, there is a pronounced alveolar congestion and lymphocyte hyperplasia in lungs.



a)

Fig. 1. Brain Tissue. a) with Normal Neurones (NU) and Nerve Fibres (F).



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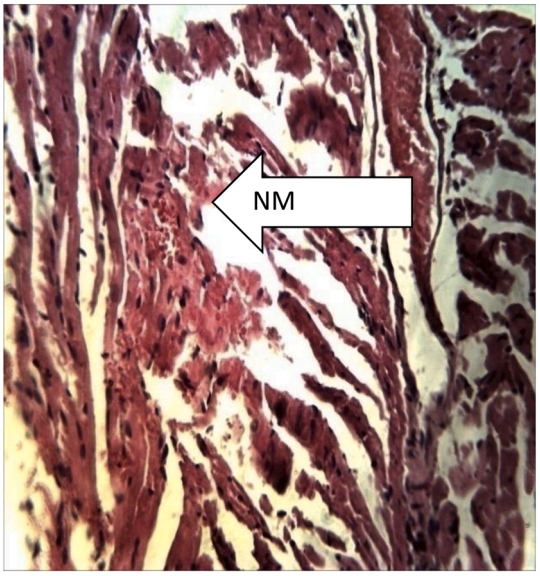

b)

Fig. 2. Heart Tissue, a) with Normal Myocardium (M); b) Heart Tissue with Slight Necrosis (N) of Myocardium (NM).

4. Discussion

Metal welding fumes having contained a relative concentration of a variety of heavy metals have induced several histopathological damages to tissues which were observed. The fumes normally pass through the respiratory tract down into the body system inducing damages to the lungs and airways. However, the respiratory system possesses defensive mechanisms and barriers from inorganic dusts. Though relatively larger particles are trapped by the nasal mucosa, others became discarded by the respiratory tract's mucociliar mechanisms and equally by the macrophages in the alveolar parencyhma of the lung. Particles that range between 1−5 μm in diameter have the ability to reach the lung parenchyma. However, smaller than 1 μm particles or dusts are removed by exhalation. The collected metal welding fumes in the present study were found to be in the respirable size range with a count mean diameter of <1 μm which portrays probable accumulation in lungs as observed in a similar published work of the same authors [9]. Some recent studies on pathology from studies of heavy metal poisoning which include cobalt, carbide, titanium, tantalum, lead and aluminium have revealed hyperplastic alveolar epithelium and fibrosis in the lung tissue including asthma and pneumonia [25] which were same observations made in present study on rats exposed to medium and high doses of metal

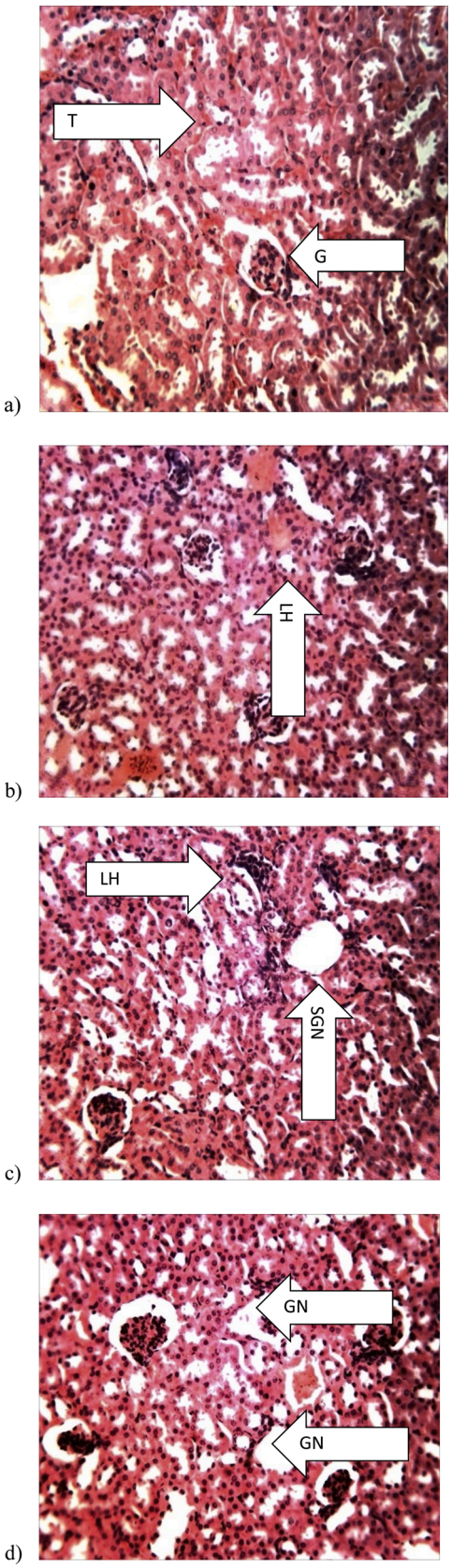

Fig. 3. Kidney Tissue, a) with Normal Tubules (T) and Glomerulus (G); b) with Slight Lymphocyte Hyperplasia (LH); c) with Slight Glomerular Necrosis (SGN) and Lymphocyte Hyperplasia (LH); d) with Moderate Glomerular Necrosis (GN).

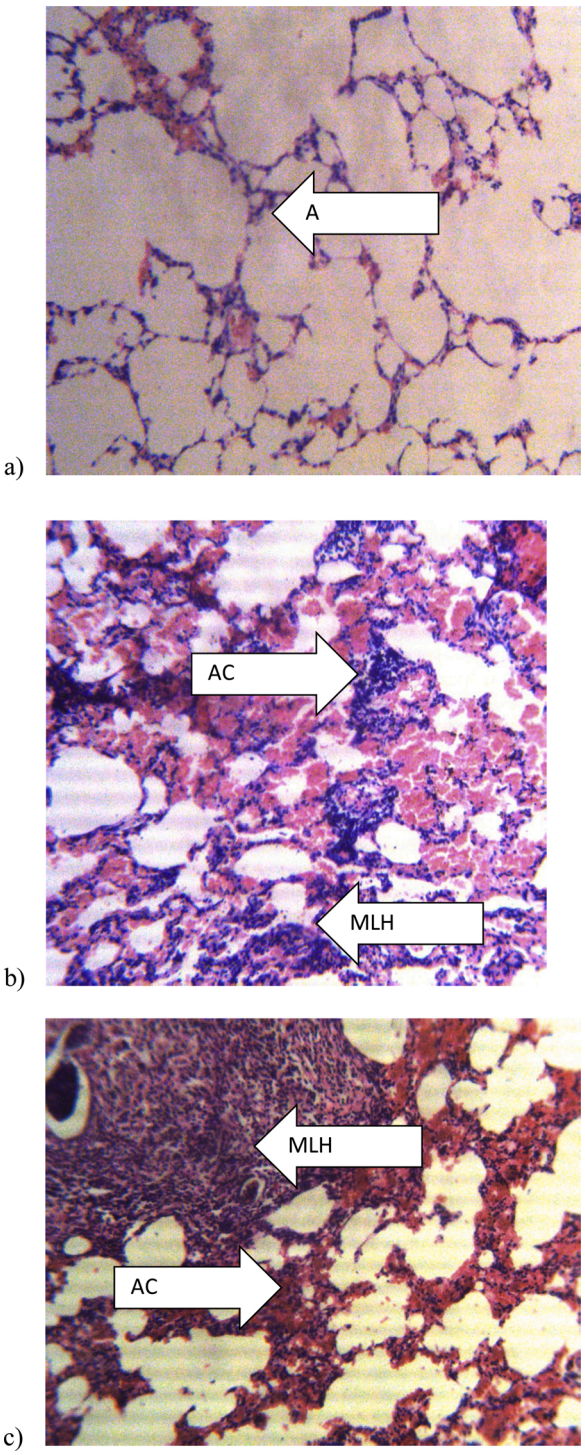

Fig. 4. Lungs Tissue, a) with Normal Alveoli (A); b) with Moderate Lymphocyte Hyperplasia (LH) with Alveoli Congestion (AC); c) with Alveoli Congestion (AC) with Moderate Lymphocyte Hyperplasia (LH).

welding fumes. The same welding fumes used for this present study was found to contain lead, cobalt, cadmium, nickel, manganese, zinc, chromium, aluminium, copper and magnesium [9]. Some of these metals such as chromium have been implicated in development of respiratory problems such as bronchitis, irritation, and possible lung cancer. Metals are suggested to play a dramatic role in inducing acute toxicity effects on epithelial cells of alveoli [26]. The resultant effects from heavy metal dusts exposure are mostly necrosis, interstitial fibrosis and degenerative changes in the lungs which were same with the present study's

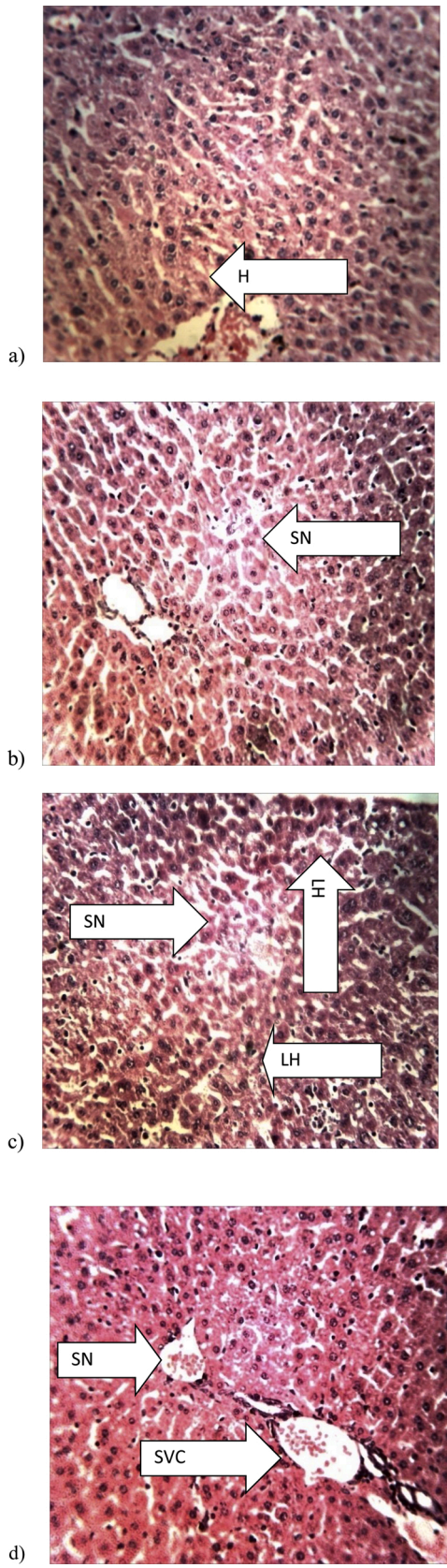

Fig. 5. Liver Tissue, a) with Normal Hepatocytes (H); b) with Slight Necrosis (SN); c) with Slight Necrosis (N) and Lymphocyte Hyperplasia (LH); d) with Slight Vascular Congestion (SVC) and Slight Necrosis (SN).

Table 2
Histopathological features in organs of Test Animals Exposed to Doses of Worker's 2 h Daily Burden for Various Years.

Test animal Groups	Brain	Heart	Kidney	Liver	Lung
IA (3yrs)	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)
IB (5yrs)	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)
IC (10yrs)	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)
ID (20yrs)	NU & NF (100 %)	NM (100 %)	SLH (71 %)	SN & LH (71 %)	MLH & AC (71 %)
Control	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)

Key: NU & NF- Neurons and Nerve fibres; NM- Normal myocardium; NG & NT- Normal glomerulus and Normal tubules; SLH- Slight lymphocyte hyperplasia; NH- Normal hepatocytes; SN- Slight necrosis; LH- Lymphocyte hyperplasia; NA- Normal alveoli; MLH- Moderate lymphocyte hyperplasia; AC- Alveoli congestion.

Table 3
Histopathological features in organs of Test Animals Exposed to Doses of Worker's 4 h Daily Burden for Various Years.

Test animal Groups	Brain	Heart	Kidney	Liver	Lung
IIA (3yrs)	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)
IIB (5yrs)	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)
IIC (10yrs)	NU & NF (100 %)	NM (100 %)	SLH (71 %)	SN & LH (86 %)	MLH & AC (86 %)
IID (20yrs)	NU & NF (100 %)	SNM (86%)	SGN & LH (100 %)	SN & LH (86 %)	MLH & AC (100 %)
Control	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)

Key: NU & NF- Neurons and Nerve fibres; NM- Normal myocardium; SNM- Slight necrosis of myocardium; NG & NT- Normal glomerulus and Normal tubules; SLH- Slight lymphocyte hyperplasia; NH- Normal hepatocytes; SN- Slight necrosis; SGN- Slight glomerular necrosis; LH- Lymphocyte hyperplasia; NA- Normal alveoli; MLH- Moderate lymphocyte hyperplasia; AC- Alveoli congestion.

Table 4
Histopathological features in organs of Test Animals Exposed to Doses of Worker's 8 h Daily Burden for Various Years.

Test animal Groups	Brain	Heart	Kidney	Liver	Lung
IIIA (3yrs)	NU & NF (100 %)	NM (100 %)	SLH (100 %)	SN & LH (100 %)	MLH & AC (100 %)
IIIB (5yrs)	NU & NF (100 %)	NM (100 %)	SLH (100 %)	SN & LH (100 %)	MLH & AC (100 %)
IIIC (10yrs)	NU & NF (100 %)	SNM (100 %)	SGN & LH (100 %)	SN & LH (100 %)	MLH & AC (100 %)
IIID (20yrs)	NU & NF (100 %)	SNM (100 %)	MGN & LH (100 %)	SVC & SN (100 %)	LH & AC (100 %)
Control	NU & NF (100 %)	NM (100 %)	NG & NT (100 %)	NH (100 %)	NA (100 %)

Key: NU & NF- Neurons and Nerve fibres; NM- Normal myocardium; SNM- Slight necrosis of myocardium; NG & NT- Normal glomerulus and Normal tubules; SLH- Slight lymphocyte hyperplasia; NH- Normal hepatocytes; SN- Slight necrosis; SGN- Slight glomerular necrosis; MGN- Moderate glomerular necrosis; LH- Lymphocyte hyperplasia; NA- Normal alveoli; MLH- Moderate lymphocyte hyperplasia; SVC- Slight vascular congestion; AC- Alveoli congestion.

observations. Some repeated inhalation investigations on rats revealed histopathological symptoms of respiratory irritation, such as discharge of mucus production by the alveoli and mucosal cells hyperplasia in the

bronchial epithelium, which were observed in rats exposed to MMA-SS fumes [27]. These were in agreement with the findings of the present study whereby alveolar lymphocyte hyperplasia and necrosis were observed in various groups exposed to varying levels of fumes and the severity was related to the respective dose levels. Similarly, Solano-Lopez et al. [28] reported hyperplasia of bronchiolo-alveoli which includes alveolar BAH and bronchiolar BAH.

Many investigations have showed that exposure to metals including Hg, Pb, Cu and Cd has induced various damages to the hepatic tissue in laboratory animals [29,30]. Some of these metals were studied in fumes used for this study as reported by Abdullahi & Sani [9]. Garg et al. [31] demonstrated that after rats were treated with Hg, there were several signs of the liver damages observed which include advance hepatocellular necrosis, disarrangement of hepatic strands, rupture in hepatocytes, dilation and congestion of blood vessels with haemorrage, dense lymphocytic infiltration round the central vein and dark strained hepatocytic nuclei indicating cell pycnosis. Some of these were among the observations reported in this study.

In addition, Bhattacharjee et al. [32] revealed that following exposure to composite metals, there were vacuolation, fatty degeneration and congestion in some liver cells. In kidney, the effects include glomerulus congestion, tubular degeneration, focal area of coagulative necrosis and exfoliated epithelium.

Lead nitrate is a metal salt and a major component of welding fumes could interact with proteins and enzymes of the hepatic interstitial tissue. By that, they affect the defense mechanisms of antioxidant resulting in production of reactive oxygen species which would subsequently induce hepatic damage [33]. Similarly, Gidlow [34], has revealed that following high exposure to Pb, there could be renal tubular damage. It has equally been reported that, Pb exposure causes renal injury; because the absorbed Pb is primarily excreted by the kidney [35]. In support of this view, some researchers have revealed that exposure to low doses of lead acetate over a long duration induce only mild to moderate renal fibrosis and tubular atrophy and the influence of doses have been positive also in this study. Also, Cd been another relative component of the welding fumes has indirectly been related with oxidative stress and tissue damage [36]. Results from Oluseye et al. [37] who examined the internal organs of Catfish (*Clarias gariepinus*) and Tilapia (*Oreochromis niloticus*) exposed to contamination by heavy metals and the kidney showed symptoms of coagulated necrosis in the renal tubules.

Many other histological studies on liver have presented that changes resulting from Cd exposure are characterized by enlarged nuclei, cellular hypertrophy, hepatocyte vacuolization, hepatocyte necrosis including dilated central vein [38] and were similar to the findings of the present study following exposure to metal welding fumes.

Mahboob et al. [39] stated that histopathological observations in kidney of Nile tilapia (*Oreochromis niloticus*) from freshwater reservoir that contained traces of heavy metals showed congestion, dilation in bowman capsule space, necrosis which were similar to some part of the presents study's findings. In support of this, evident pathological changes were observed in the small vessels of various tissues and organs among which [40] reported similar changes in rat's liver following administration of 6 mg Cd/kg of body weight and confirmed that the liver was the major primary target organ for acute cadmium toxicity. This in turn is supported by the fact that cadmium initially accumulates in the liver prior to translocation to the kidney.

It has also been found that, Cd toxicity has induced pulmonary, skeletal, renal, reproductive, hepatic and cardiovascular dysfunction [41–43]. This was in agreement with the results of Tsao et al. [44] that also found similar findings in rats and reported that excessive exposure to Pb is associated with cardiomyopathy. These results are in line with findings of Fell [45], who stated that the severity of lead effects on cardiovascular system tend to be affected by the dose and exposure duration. The same observations were made in this study whereby the severity of the effects becomes directly related to the dose levels.

Several other studies have implicated some heavy metals examined in the welding fumes of this present study in various histological damages in fishes. Saini [46] has recorded severe histopathological lesions such as infiltration of lymphonuclear cells, degeneration of hepatic parenchyma and deformation of hepatocytes caused by heavy metals. Likewise, Chavan & Muley, [47] found congestion in sinusoids, cytoplasmic vacuolation, venules and focal necrosis following exposure of *Cirrhina mrigala* to sub-lethal levels of lead acetate. In addition, Jalaludeen et al. [48] observed several clear changes which include severe damage, marked proliferation of ducted cells, and conversion of liver tissue into sponge mass and large vacuoles in liver tissue of *Tilapia mossambica* following administration of cadmium sulphate. Patnaik et al. [49] equally observed hypertrophy of hepatocytes, vacuolation and accumulation of metals in liver of *Cyprinus carpio* treated with Pb and Cd. Complete disintegration of liver tissue and marked necrosis was detected by Mary et al. [50] in *C. mrigala* following exposure to lead nitrate. Moreover, various alterations such as mild edema, reduction in cell size, severe damage and further degeneration of renal tubules, disorganization of renal tissue and necrosis were noticed when *T. mossambica* was exposed to sub-lethal concentration of cadmium sulphate for 20 days under laboratory conditions [48]. Likewise, Rana et al. [51] noted various changes such as aggregation of inflammatory cells, dilation in capillary tubes of renal tubules and hemolysis in kidney of *C. carpio*, following exposure to chromium at sub-lethal levels. Chromium is one of the dominant metals in the fumes used for the present study as revealed by Abdullahi & Sani [9] and damages to the kidney were observed which include lymphocyte ghyperplasia and glomerular necrosis. These findings were in accordance with the results of Saini [46], that noticed pathological changes which include vacuolar degeneration, congestion of blood vessels and degeneration of tubules in the kidney of fish *L. rohita* procured from from freshwaters of Punjab. It was also stated that histopathological observations of Liver of the of *Oreochromis niloticus* from freshwater reservoir that contained traces of heavy metals showed cytoplasmic vacuolation, necrosis, sinusoid dilation Mahboob et al. [39]. This was same as results from Oluseye et al. [37], who examined some internal organs of catfish and tilapia exposed to contamination of heavy metals and the liver's hepatocytes showed foamy appearance and large-sized vacuoles.

5. Conclusion

The study reveals unaffected brain tissues in all treated animals. However, lymphocyte hyperplasia and necrosis were noticed in heart, kidney, liver and lungs tissues which became more obvious at higher doses. Thus, exposure to metal welding fumes have caused damages that have translated into lesions and several pathologies in kidney, lungs, liver and heart tissues. The kidney liver and lungs were the most affected starting from the least concentration of 51.46 mg/rat. Regulation and control should be imposed on exposure to welding fumes by metal workers.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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