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IMPACTS OF CHRONIC CIGARETTE SMOKE EXPOSURE ON LUNG HISTOLOGY AND OXIDATIVE STRESS MARKERS IN ADULT MALE WISTAR RATS

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ABSTRACT

Purpose: Cigarette smoke contains numerous toxic and carcinogenic compounds capable of inducing oxidative stress and structural damage to lung tissue. This study evaluated the effects of chronic cigarette smoke exposure on lung histology and oxidative stress markers in adult male Wistar rats. **Methods**: Forty adult male Wistar rats were randomly assigned into four groups (n = 10): control (feed and water only), and three smoke-exposed groups subjected to six sticks of cigarette smoke for 30, 60 or 120 minutes daily for 28 days using a whole-body exposure chamber. Body weight and relative lung weight were recorded. Oxidative stress markers, malondialdehyde (MDA) and superoxide dismutase (SOD), were assessed. Lung tissues were processed for histological examination using hematoxylin and eosin staining. **Results**: Chronic smoke exposure produced a non-significant increase in body weight but reduced relative lung weight compared with control rats. MDA levels were significantly elevated in rats exposed for 30 and 120 minutes ($p < 0.05$), while SOD activity was significantly reduced across all smoke-exposed groups ($p < 0.05$). Histological findings showed mild to moderate focal alveolar fluid exudation with preservation of alveolar architecture. **Conclusion**: Chronic cigarette smoke exposure induces oxidative stress and mild histopathological alterations in the lungs of adult male Wistar rats, supporting the toxic effect of cigarette smoke on pulmonary tissue.

KEYWORDS: Cigarette smoke; Oxidative stress; Lung histology; Wistar rats; Malondialdehyde.

INTRODUCTION

Cigarette smoking remains one of the leading preventable causes of morbidity and mortality worldwide. Tobacco smoke contains more than 9,500 chemical compounds, including reactive oxygen species, aldehydes, heavy metals and numerous carcinogens, many of which exert direct toxic effects on the respiratory system.[1,2] Chronic inhalation of cigarette smoke has been strongly associated with the development of chronic obstructive pulmonary disease (COPD), lung cancer and other respiratory disorders.[3]

The lungs are particularly vulnerable to smoke-induced injury because they are the primary site of exposure. Repeated inhalation of cigarette smoke leads to persistent airway inflammation, oxidative stress and structural remodeling of lung tissue. Oxidative stress plays a central role in this process by overwhelming endogenous antioxidant defence mechanisms, resulting in lipid peroxidation, protein oxidation and DNA damage.[4] Malondialdehyde (MDA) is commonly used as a biomarker of lipid peroxidation, while superoxide dismutase (SOD) represents a key enzymatic antioxidant that protects tissues against oxidative damage.[5]

Although epidemiological studies in humans have clearly demonstrated the harmful effects of smoking, controlled experimental studies are essential for understanding the underlying mechanisms of smoke-induced lung injury. Animal models allow for standardized exposure conditions and direct assessment of biochemical and histological changes. Wistar rats are widely used in respiratory toxicology research because of their physiological similarity to humans and their reproducible response to inhaled toxicants.[6]

Despite existing evidence, there is still a need for experimental data that links chronic cigarette smoke exposure with oxidative stress and structural alterations in lung tissue under controlled conditions. Therefore, this study was designed to investigate the effects of chronic cigarette smoke exposure on lung histology and oxidative stress markers in adult male Wistar rats.

METHODS

Ethical approval

Ethical approval for this study was obtained from the Animal Ethics Committee, Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi Campus, in accordance with the principles of laboratory animal care and use.

Experimental animals

Forty (40) adult male Wistar rats weighing between 150 and 200 g were obtained from the Animal House of the Department of Human Physiology, Nnamdi Azikiwe University, Nnewi Campus. The animals were housed in standard cages under controlled environmental conditions (temperature 27 ± 2 °C, 12-h light/dark cycle) and were allowed free access to standard laboratory feed and water ad libitum. The rats were acclimatized for three weeks before the commencement of the experiment.

Experimental design

The rats were randomly divided into four groups (n = 10 per group).

Group A (Control): Received standard feed and water only
Group B: Exposed to cigarette smoke for 30 minutes daily
Group C: Exposed to cigarette smoke for 60 minutes daily
Group D: Exposed to cigarette smoke for 120 minutes daily

Smoke exposure was carried out using a whole-body exposure chamber. Rats in the exposed groups were subjected to smoke from six sticks of cigarettes daily for 28 consecutive days.

Sample collection

At the end of the exposure period, the animals were sacrificed under appropriate anaesthesia. The lungs were excised, blotted dry and weighed to determine relative lung weight. Blood samples were collected for oxidative stress analysis. Lung tissues were fixed for histological examination.

Biochemical analysis

Oxidative stress markers were assessed using standard laboratory methods. Malondialdehyde (MDA) levels were measured as an index of lipid peroxidation, while superoxide dismutase (SOD) activity was determined to assess antioxidant status.

Histological analysis

Lung tissues were fixed in 10 % neutral buffered formalin, processed routinely, embedded in paraffin wax and sectioned at 4–5 µm thickness. Sections were stained with hematoxylin and eosin (H&E) and examined under a light microscope for histopathological changes.

Statistical analysis

Data were analysed using one-way analysis of variance (ANOVA) followed by least significant difference (LSD) post-hoc test. Results were expressed as mean ± standard error of mean (SEM). Statistical significance was set at $p < 0.05$.

RESULTS

Table 1: Effect of cigarette smoke exposure on body weight.

	Initial weight (g)	Final weight (g)	p-value	t-value
	MEAN±SEM	MEAN±SEM		
Group A (control)	118.00±2.00	121.00±9.00	0.776	0.325
Group B	147.30±12.25	190.30±31.12	0.268	1.286
Group C	148.00±11.36	180.67±10.89	0.107	2.075
Group D	164.33±8.51	193.00±17.35	0.212	1.483

Data was analysed using t-test using Graph-pad Prism 9.5.1, and values were considered significant at $p \leq 0.05$.

The mean body weight result in table 1 reveals an increase in groups A, B, C, and D when the initial weight was compared to the final weight, which had no significant difference.

Table 1 shows the effect of chronic cigarette smoke exposure on the body weight of adult male Wistar rats. There was an increase in final body weight in both control and smoke-exposed groups when compared with their initial body weight. However, the observed increase in body weight among the smoke-exposed groups was not statistically significant when compared with the control group ($p > 0.05$).

Table 2: Effect of cigarette smoke exposure on relative lung weight.

	Rel. lungs weight (g)
	MEAN±SEM
Group A (control)	0.84±0.04
Group B	0.67±0.08
Group C	0.72±0.03
Group D	0.77±0.03
F-ratio	1.918

Data was analysed using ANOVA followed by post Hoc LSD multiple comparison, and values were considered significant at $p \leq 0.05$. *: significant.

Table 2 result showed a decrease in the relative lungs weight in groups B, C, and D (p=0.052,p=0.150,p=0.407) compared to group A, which indicate no statistical significance.

As shown in **Table 2**, chronic cigarette smoke exposure resulted in a reduction in relative lung weight in all smoke-exposed groups compared with the control group. Although the decrease was more pronounced in the smoke-exposed groups, the difference was not statistically significant ($p > 0.05$).

Table 3: Effect of cigarette smoke exposure on oxidative stress markers.

	MDA level (nmol/ml)	SOD level (U/L)
	MEAN±SEM	MEAN±SEM
Group A (control)	1.11±0.01	18.63±0.22
Group B	1.35±0.01*	8.20±0.58*
Group C	1.16±0.02	11.67±0.73*
Group D	1.26±0.03*	9.52±0.76*
F-ratio	22.253	57.23

Data was analysed using ANOVA followed by post Hoc LSD multiple comparison, and values were considered significant at $p \leq 0.05$. *: significant.

Table 3 reveals a significant increase in the MDA levels in groups B (p=0.001) and D (p=0.001), group C (p=0.152) had an increase but was not significant when compared to group A. In addition, the SOD level indicated a significant decrease in groups B, C, and D (p=0.001, p=0.001, p=0.001) compared to group A.

The effect of cigarette smoke exposure on oxidative stress markers is presented in **Table 3**. Rats exposed to cigarette smoke showed a significant increase in malondialdehyde (MDA) levels, particularly in the 30-minute and 120-minute exposure groups, compared with the control group ($p < 0.05$). In contrast, superoxide dismutase (SOD) activity was significantly reduced in all smoke-exposed groups when compared with the control group ($p < 0.05$).

Histological findings

Histological examination of lung tissues from the control group showed normal lung architecture with intact alveolar spaces and thin alveolar septa. In contrast, lung sections from smoke-exposed rats revealed mild to moderate focal alveolar fluid exudation. Despite these changes, the general alveolar architecture and septal outlines remained largely preserved across all smoke-exposed groups.

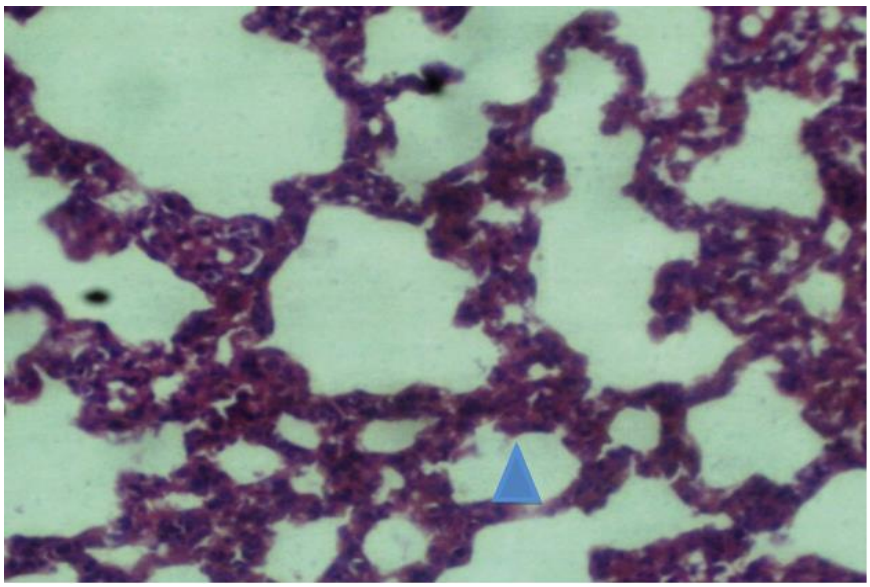

Plate 1: Photomicrograph of lung tissue from the control group showing normal lung parenchyma with intact alveolar spaces, thin alveolar septa and normal alveolar architecture. Hematoxylin and eosin stain, ×400.

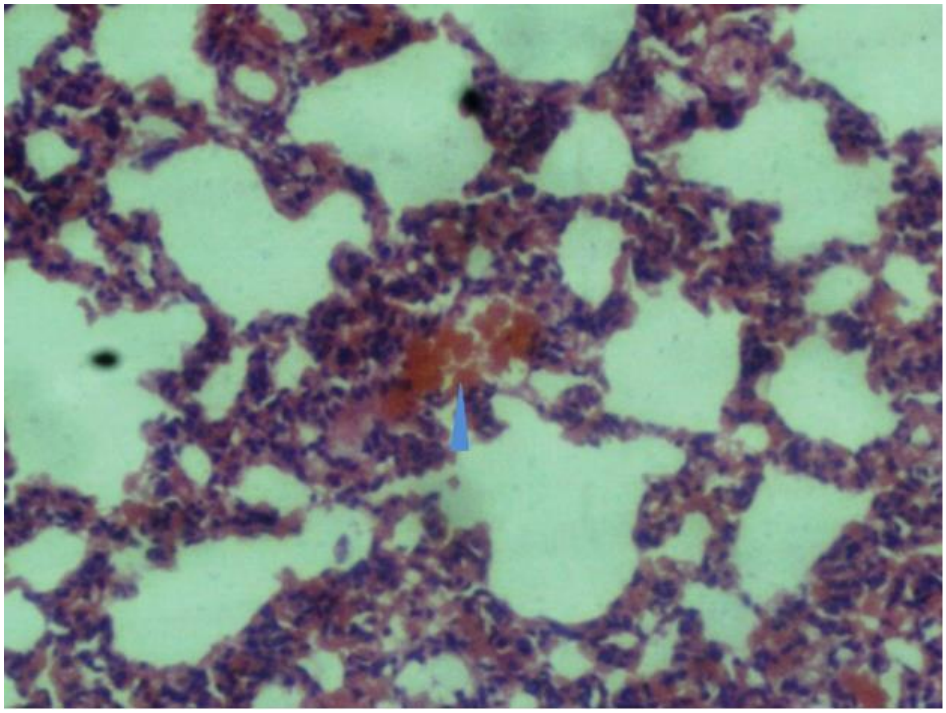

Plate 2: Photomicrograph of lung tissue from rats exposed to cigarette smoke for 30 minutes showing mild focal alveolar fluid exudation with partial filling of alveolar spaces. The alveolar architecture remains preserved. Hematoxylin and eosin stain, ×400.

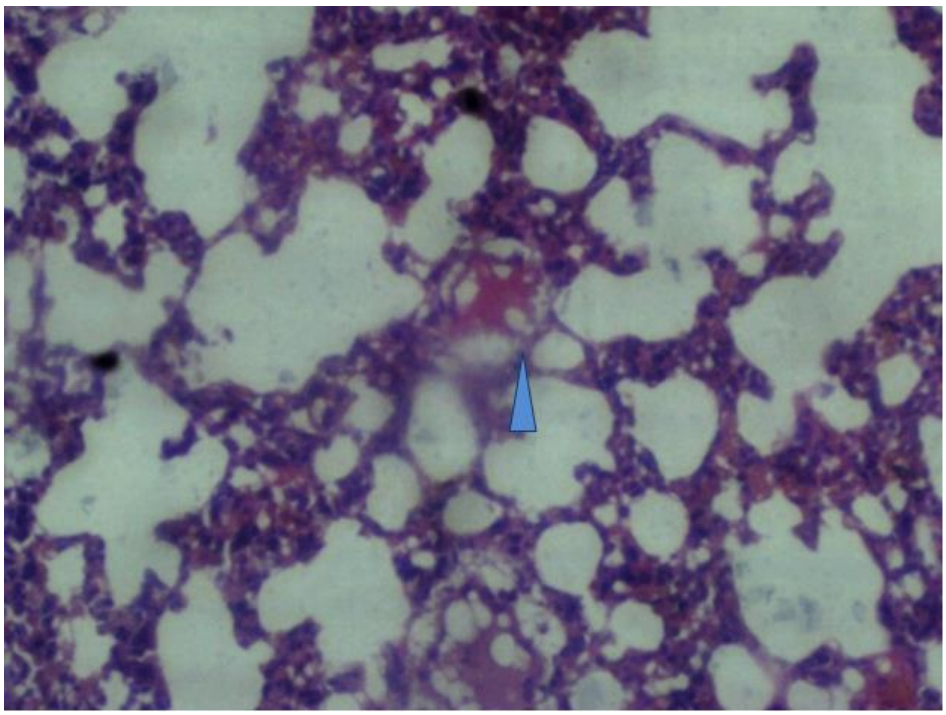

Plate 3: Photomicrograph of lung tissue from rats exposed to cigarette smoke for 60 minutes showing moderate focal alveolar fluid exudation and partial obliteration of some alveolar spaces, with preserved septal outlines. Hematoxylin and eosin stain, ×400.

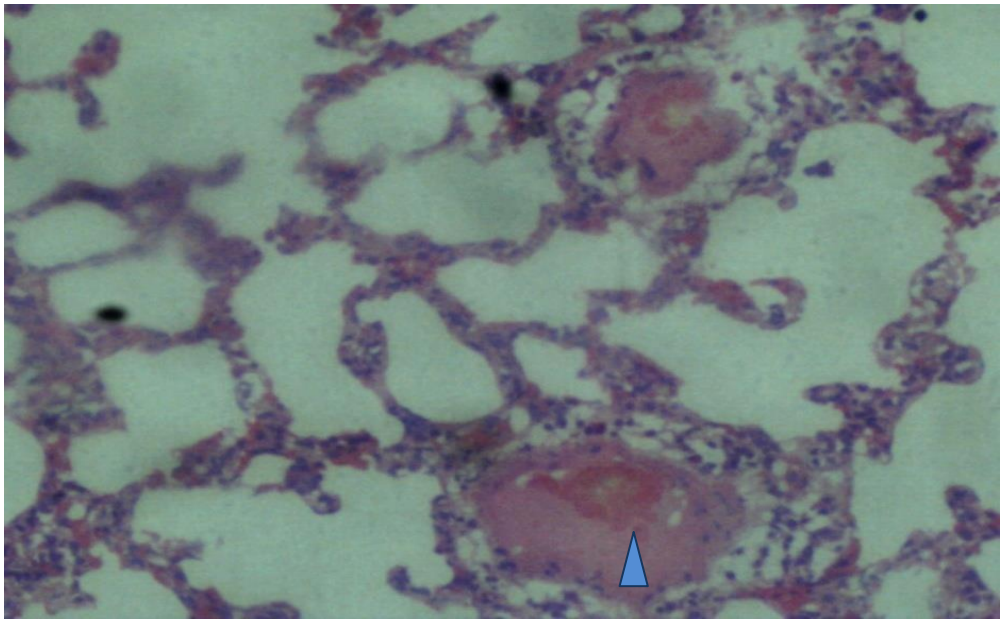

Plate 4 (1): Photomicrograph of lung tissue from rats exposed to cigarette smoke for 120 minutes showing mild to moderate alveolar fluid infiltration with maintained alveolar structure and septal integrity. Hematoxylin and eosin stain, ×400.

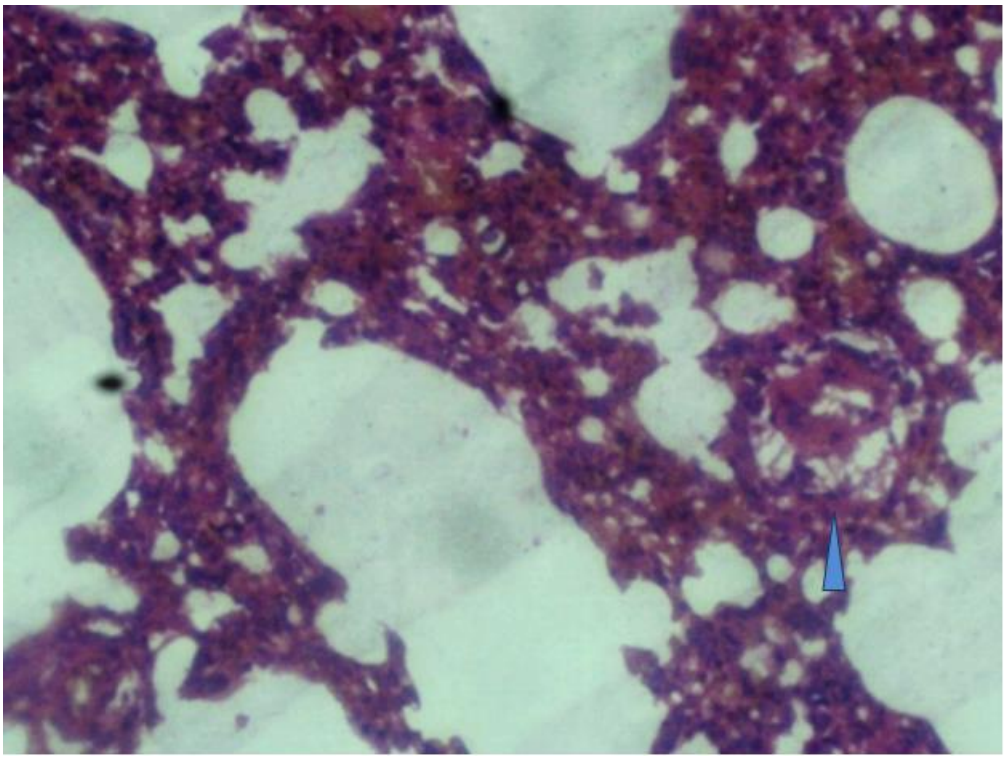

Plate 4 (2): A photomicrograph shows a section of lung tissue with mild focal fluid exudation in some of the alveolar sacs. The exudates appear pale, eosinophilic with proteinaceous material filling portions of the alveolar lumens, causing partial obliteration of the alveolar spaces (arrow). However, the alveolar architecture remains recognisable, with preserved septal outlines and alveolar borders (H&E x 400).

DISCUSSION

This study investigated the effects of chronic cigarette smoke exposure on lung histology and oxidative stress markers in adult male Wistar rats. Cigarette smoke contains numerous toxic substances capable of inducing oxidative stress, inflammation and tissue injury, particularly in the lungs, which are the primary site of exposure.[1,2]

The present findings showed that chronic cigarette smoke exposure produced a non-significant increase in body weight in exposed rats compared with the control group. Although smoking has often been associated with

reduced body weight, variations in exposure duration, animal age and metabolic responses may explain the observed weight changes in this study. Similar observations have been reported in experimental studies where prolonged smoke exposure did not significantly alter body weight.[7]

Relative lung weight was reduced in smoke-exposed rats compared with control animals, although the reduction did not reach statistical significance. Decreased lung weight may reflect tissue injury, alveolar damage or loss of cellular integrity following prolonged exposure to cigarette smoke. Previous studies have reported comparable reductions in lung weight following chronic smoke exposure, which have been attributed to structural damage and oxidative injury.[8]

Oxidative stress analysis revealed a significant increase in malondialdehyde levels in smoke-exposed rats, particularly in the 30- and 120-minute exposure groups. Elevated MDA levels indicate enhanced lipid peroxidation resulting from excessive generation of reactive oxygen species. In contrast, superoxide dismutase activity was significantly reduced in all smoke-exposed groups, suggesting depletion of endogenous antioxidant defences. These findings are consistent with earlier reports demonstrating that cigarette smoke overwhelms antioxidant systems and promotes oxidative lung injury.[4,9]

Histological examination further supported the biochemical findings. Lung tissues from control rats displayed normal alveolar architecture, while smoke-exposed rats showed mild to moderate focal alveolar fluid exudation. Despite these changes, the overall alveolar structure and septal outlines were largely preserved, indicating early-stage lung injury rather than advanced emphysematous destruction. Similar histopathological changes have been documented in experimental models of chronic cigarette smoke exposure.[10]

Overall, the findings of this study confirm that chronic cigarette smoke exposure induces oxidative stress and mild histopathological alterations in lung tissue, reinforcing the role of oxidative mechanisms in smoke-related pulmonary toxicity.

CONCLUSION

This study demonstrated that chronic cigarette smoke exposure induces oxidative stress and mild histopathological alterations in the lungs of adult male Wistar rats. Increased malondialdehyde levels and reduced superoxide dismutase activity indicate enhanced lipid peroxidation and depletion of antioxidant defences following smoke exposure. Histological findings revealed mild to moderate focal alveolar fluid exudation with preservation of overall alveolar architecture.

These findings confirm the toxic effect of chronic cigarette smoke on lung tissue and highlight oxidative stress as a key mechanism underlying smoke-induced pulmonary injury.

DECLARATIONS

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. UJC conceived and designed the study, carried out the experiments and drafted the manuscript. OOC supervised the study, analysed the data and revised the manuscript. All authors read and approved the final manuscript for publication.

Ethical Approval

Ethical approval for this study was obtained from the Animal Ethics Committee, Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi Campus, in accordance with guidelines for the care and use of laboratory animals.

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Use of Artificial Intelligence/Large Language Models

Artificial intelligence-based tools were used for language editing and formatting of the manuscript only. No AI system was used for data generation, analysis or interpretation.

Use of Research Reporting Tool

The ARRIVE guidelines from the EQUATOR Network were consulted during the design and reporting of this animal study.

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