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Systemic Inflammatory and Genotoxic Effects of Shisha Smoking: A Case Control Study in Yenagoa, Bayelsa State, Nigeria

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ABSTRACT

Background: Shisha smoking is linked to oxidative stress and vascular inflammation, which are vital factors in the pathophysiology and advancement of respiratory and cardiovascular disorders, as well as cancer.

Objective: This study evaluated and compared systemic inflammatory biomarkers and DNA damage markers between shisha, cigarette, dual, and second-hand shisha smokers and non-smokers.

Methods: A case-control study approach was employed involving 150 individuals aged between 16 and 35 years. Participants were divided into five categories: shisha smokers (n=30), cigarette smokers (n=30), dual (both) smokers (n=30), secondhand shisha smokers (n=30), and nonsmokers (n=30). Venous blood samples were obtained and assessed for systemic inflammatory and DNA damage biomarkers using enzyme-linked immunosorbent assay. Data analysis was done with the Statistical Package for Social Sciences (SPSS), with the significance level set at $p < 0.05$.

Results: Compared with the non-smokers, the serum levels of interleukin-6 (IL-6), C-reactive protein (CRP), 8-nitroguanine (8-NO_2-Gua), and malondialdehyde were higher ($p<0.05$) in shisha smokers, cigarette smokers, and both smokers and secondhand smokers. Serum IL-6, CRP, 8NO_2-Gua, 4-HNE, and MDA levels were slightly higher in shisha smokers than cigarette smokers. Both smokers exhibited significantly higher ($p < 0.05$) levels of IL-6, CRP, 8NO_2-Gua, and MDA than exclusive shisha or cigarette smokers.

Conclusion: The study found that shisha and cigarette smokers had higher levels of indicators of systemic inflammation, oxidative stress, and DNA damage. It also confirmed that smoking cigarettes and shisha concurrently is more harmful than smoking either shisha or cigarettes alone.

Keywords: DNA Damage Markers, Systemic Inflammation, Shisha Smoking, Cigarette Smoking.

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INTRODUCTION

Tobacco use continues to be a significant global public health issue, leading to more than 5 million avoidable deaths each year worldwide [1]. Although cigarette use has been recognized as a crucial health hazard, other means of tobacco use, particularly shisha smoking, have become very popular, especially among adolescents and young adults. This increasing trend is mainly driven by the misconception that shisha smoking is a safer option than cigarettes. Nevertheless, a growing body of scientific evidence contradicts this notion, showing that shisha smoking poses similar acute and chronic health dangers [2,3].

Shisha smoke is a complex aerosol containing various toxic and carcinogenic substances, including polycyclic aromatic hydrocarbons, volatile organic compounds, nicotine, aldehydes, carbon monoxide, and heavy metals, many of which can also be found in cigarette smoke [4,5]. It has been demonstrated that exposure to these toxins negatively impacts the immunological and respiratory systems and causes genetic mutation. Beyond inflammatory injury, exposure to tobacco smoke is one of the most important and avoidable ways that people are exposed to genotoxic and carcinogenic substances. These substances exert deleterious effects through oxidative stress, DNA damage, carbon monoxide toxicity, and the accumulation of heavy metals, collectively promoting genomic instability and carcinogenesis [6].

Systemic inflammation is a well-known pathological mechanism underlying the advancement of several chronic disorders, such as cancer, cardiovascular disease, acute myocardial infarction, stroke, and coronary artery disease [7]. According to Gouveia et al. [8], acute shisha smoking triggers inflammatory reactions marked by increased levels of circulating leukocytes, such as monocytes, lymphocytes, neutrophils, and eosinophils. These immunological disruptions may develop into persistent low-grade systemic inflammation with prolonged exposure, which is identified to contribute to the onset of chronic non-communicable diseases [8]. Long-term shisha smoking has also been linked to skeletal muscle atrophy, aberrant inflammatory reactions in the lungs, and functional impairment, especially in diseases like chronic obstructive pulmonary disease (COPD) [9].

Interleukin-6 (IL-6) and C-reactive protein (CRP) are two of the most extensively researched indicators of systemic inflammation. While circulating CRP is a sensitive indicator of inflammatory status and tissue damage, interleukin-6 is an important proinflammatory cytokine and a major regulator of hepatic CRP synthesis [10,11]. Chronic exposure to tobacco smoke further amplifies oxidative and nitrosative stress, creating a biological environment conducive to persistent DNA damage and inflammatory signaling.

Genotoxicity refers to alteration in DNA structure or segregation, including DNA fragmentation and DNA migration. Its association with tobacco use has been strongly linked to mutations in critical regulatory genes, such as the p53 tumor suppressor gene, which is vital for maintaining genomic integrity and regulating cell cycle progression. Alterations in p53 are found in over 50% of all human cancers and lead to unregulated cell growth and tumor formation [12]. Besides inflammatory biomarkers, markers of oxidative stress-related DNA damage offer essential understanding of the biological effects of tobacco exposure.

4-Hydroxynonenal is a reactive lipid peroxidation by-product from polyunsaturated fatty acids and acts as a strong marker of oxidative damage to cell membranes. Although low levels of 4-HNE are involved in cellular signaling and regulatory pathways, high concentrations lead to protein modification, DNA damage, and irreversible cellular harm [13,14]. Similarly, 8-nitroguanine is a mutagenic DNA damage formed during prolonged inflammatory states via interactions between guanine bases and reactive nitrogen species like peroxynitrite. This lesion represents a considerable proportion of steady-state oxidative DNA damage and has been observed at increased levels in critical organs of test animals subjected to tobacco smoke [15,16].

Shisha smoking is becoming more common in Nigeria, especially among young individuals, although there is still a dearth of localized biochemical evidence evaluating its genotoxicity and systemic inflammation. Early risk identification and public health management depend on an understanding of these fundamental changes. Therefore, this study evaluated and compared systemic inflammatory biomarkers (interleukin-6 and C-reactive protein) and DNA damage markers (8-Nitroguanine and 4-hydroxynonenal) among shisha smokers, cigarette smokers, combined shisha and

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cigarette smokers, second-hand shisha smokers, and non-smoking individuals in Yenagoa, Bayelsa State, Nigeria.

METHODOLOGY

Study Area and Population

This study was conducted in Yenagoa town, Bayelsa State, Nigeria. Study subjects included males and females between the ages of 16 and 35 years because shisha smoking is more prevalent among adolescents and young adults in Yenagoa town, Bayelsa State, Nigeria. Participants were shisha and cigarette smokers who frequently visited socio-economic locations such as lounges, bars, ghettos, and nightclubs and had a history of regular shisha and cigarette smoking, at least twice a week in the case of shisha smokers and five cigarettes per day for two years.

Study Design

This case-control study was conducted between March 2024 and February 2025 among adolescents and young adults in Yenagoa, the capital of Bayelsa State, Southern Nigeria. A purposive stratified sampling technique was used to select the study participants. A total of 150 participants, comprising males and females aged 16 and 35 years, who had a history of regular shisha and cigarette smoking for a period of at least two years. Blood samples were collected from subjects comprising 30 shisha smokers (smoking at least 2 shisha heads twice per week), 30 cigarette smokers (smoking at least five sticks per day), 30 dual smokers (individuals who smoke both shisha and cigarette concurrently), 30 secondhand smokers (non-active smokers who work in nightclubs, bars, and lounges for at least two years in a closed space), and 30 apparently healthy non-smokers, prior to the commencement of the experiment (baseline). Thereafter, at the 6th month of smoking or exposure, blood samples were collected from all participants.

Ethical Considerations

The study received ethical approval from the Research and Ethics Committee of the Bayelsa State Ministry of Health (Approval No: BSHREC/Vol. 1/24/03/04) prior to commencement. Prior to recruitment, participants were fully briefed on the study objectives, data acquisition processes, sample collection techniques, and potential effects. Participation was entirely voluntary, confidentiality was strictly maintained, and written informed consent was secured from all participants.

Sample Size

Sample size was determined using Cochran formula:

$$n = \frac{Z^2 \times p\,(1-p)}{(e)^2}$$

n= Sample size
Z= Confidence level at 95% (1.96)
p= Prevalence rate of 7.1% in Lagos, Nigeria (0.071) [17]
e= Error probability at 5% (0.05)
An initial sample size of ninety (90) subjects was obtained after considering a 10% attrition factor. The subjects were subdivided into three (3) groups comprising 30 shisha smokers, 30 shisha and cigarette smokers, and 30 secondhand shisha smokers. In addition, 30 exclusive cigarette smokers and 30 apparently healthy non-smokers were recruited as control groups, making a total of 150 participants in the study.

Selection Criteria

Inclusion criteria: Apparently healthy males and females within 16 to 35 years old who are shisha smokers (smoking at least twice a week), cigarette smokers (smoking at least five sticks per day), both smokers (individuals who used both shisha and cigarettes for a minimum of two years), secondhand shisha smokers (workers in nightclubs, bars, and lounges in a closed environment), and non-smokers who consented to take part in the study were all included for the study.
Exclusion criteria: Participants with known chronic metabolic diseases like diabetes, liver disease, renal disorders, blood disorders, chronic infection, those on medication, and those with a history of alcohol abuse, users of hard drugs, and those who did not consent to the study were excluded from the study.

Samples Collection and Preparation

Five milliliters of baseline venous blood were obtained from the antecubital vein of participants across the five study groups into plain tubes and allowed to stand undisturbed at room temperature for one hour to allow proper clotting. Following clotting, the clots were gently dislodged, and the samples were centrifuged at 1000

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revolutions per minute (rpm) for 10 minutes. The resulting serum was carefully separated and transferred into appropriately labeled plain tubes. Serum samples were kept at –20 °C in a deep freezer until analysis. All baseline samples were analyzed within 7 days of collection. After six months of consistent exposure to shisha and cigarette smoke, five milliliters of venous blood samples were collected from the same individuals following the same procedures [18]. The serum was analyzed for inflammatory markers such as C-reactive protein and interleukin-6 and DNA damage markers such as 8-nitroguanine and 4-hydroxynonenal.

Measurement of Inflammatory and DNA Damage Markers

Interleukin 6 (IL-6) was measured in accordance with the ELISA method described by Helle *et al*. [19] using the IL-6 ELISA kit (Catalog no: RD194015200R) manufactured by BioVendor–Laboratorní medicína Karásek, Brno, Czech Republic. Serum CRP was measured using a colorimetric microplate enzyme immunoassay, as described by Kindmark [20], using the Accu-bind Enzyme Immunoassay microwells kit (Product Code: 3125-300) manufactured by Monobind Inc., Lake Forest, USA. Serum malondialdehyde (MDA) was analyzed by the method reported by Onitsha et al. [21] using an autoanalyzer spectrophotometer. The DNA damage biomarkers (8-Nitroguanine and 4-Hydroxynonenal) were estimated using the enzyme-linked immunosorbent assay (ELISA) method described by Sliwinska *et al.* [22] by using the OxiSelect™ Oxidative RNA Damage ELISA Kit manufactured by Cell Biolabs, Inc., San Diego, USA.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) Version 23.0 (SPSS Inc., Chicago, IL, USA; Version 23.0) was used for all statistical analysis. One-way ANOVA was used for comparing values of the measured biochemical parameters between the control and experimental groups. All post hoc testing was done using Tukey HSD and Games-Howell methods as applicable. Data were considered significant at $p < 0.05$.

RESULTS

Tables 1 and 2 revealed that IL-6 levels were significantly elevated ($p < 0.05$) in shisha smokers, cigarette smokers, and both smokers and secondhand smokers compared to the nonsmokers. Serum IL-6 in both smokers (20.23 ± 6.20) was significantly higher ($p < 0.05$) than in shisha smokers (9.00 ± 3.46), cigarette smokers (13.88 ± 3.80), and secondhand smokers (17.57 ± 4.41). IL-6 levels in the shisha smokers were slightly higher than in cigarette smokers but insignificant ($p>0.05$). Secondhand shisha smokers also had a slight but insignificant elevation ($p>0.05$) in IL-6 levels compared to exclusive shisha smokers and cigarette smokers. CRP levels were significantly higher ($p < 0.05$) in shisha smokers, cigarette smokers, and both smokers and secondhand smokers compared to the nonsmokers. Serum CRP levels showed a significant increase ($p < 0.05$) in both smokers (2.01 ± 0.82) compared to the nonsmokers (1.15 ± 0.12). CRP levels had significant elevation in shisha smokers (1.72 ± 0.90) and all smokers (2.01 ± 0.82) compared to the nonsmokers (1.15 ± 0.12) ($p < 0.05$) (Tables 1 and 2). Biomarkers of DNA damage and oxidative stress such as 8-Nitroguanine ($8NO_2$-Gua), 4-Hydroxynonenal (4-HNE), and malondialdehyde (MDA) were measured (Tables 3 and 4). Serum 8-nitroguanine ($8NO_2$-Gua) and malondialdehyde (MDA) levels were significantly higher ($p<0.05$) in all categories of smokers compared to the nonsmokers at 6 months of smoking. There were no significant alterations in levels of 4-Hydroxynonenal (4-HNE) in shisha smokers, cigarette smokers, or both smokers and secondhand smokers compared to the nonsmokers. Seum $8NO_2$-Gua levels in cigarettes and both smokers were significantly higher than nonsmokers. Serum MDA levels in both smokers were significantly higher ($p < 0.05$) than in the nonsmokers. However, the levels of $8NO_2^-$-Gua, 4-HNE, and MDA in the cigarette smokers were slightly higher than in shisha smokers, but not significant ($p>0.05$). There were slight insignificant changes in the serum IL-6, CRP, $8NO_2$-Gua, 4-HNE, and MDA levels between the thirty male and thirty female shisha smokers (Figure 1).

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Table 1: Mean Values of Some Inflammatory Biomarker Levels in Smokers and Nonsmokers at Baseline

Parameter	Mean ± SD					*F-value*	*p-value*
	Non-smokers (n = 30)	Shisha smokers (n = 30)	Cigarette smokers (n = 30)	Both Smokers (n = 30)	Second hand smokers (n = 30)		
IL-6 (pg/ml)	9.00 ± 3.46[a]	13.59 ± 3.63 [b]	9.25 ± 2.49	19.72± 5.68 [c]	17.52 ± 4.45[bc]	27.25	0.000[***]
CRP (mg/L)	1.15 ± 0.12 [a]	1.40 ± 0.18 [b]	1.23 ± 0.28	2.01 ± 0.82 [bc]	1.76 ± 0.44	14.39	0.000[***]

Key: n = total number, SD = standard deviation, IL-6 = interleukin-6, CRP = c-reactive protein. * Values with different superscript letters (a, b, c) within the same row are significantly different from each other based on post-hoc analysis (Tukey HSD). Significant difference observed, p < 0.01.

Table 2: Mean Values of Some Inflammatory Biomarker Levels in Smokers and Nonsmokers at 6 months of smoking

Parameter	Mean ± SD					*F-value*	*p-value*
	Non-smokers (n = 30)	Shisha smokers (n = 30)	Cigarette smokers (n = 30)	Both Smokers (n = 30)	Second hand smokers (n = 30)		
IL-6 (pg/ml)	9.00 ± 3.46[a]	14.94±3.42 [b]	13.88 ± 3.80[b]	20.23 ± 6.20[c]	17.57±4.41 [bc]	18.54	0.000[***]
CRP (mg/L)	1.15 ± 0.12 [a]	1.40 ± 0.18 [b]	1.23 ± 0.28 [a]	2.01 ± 0.82 [c]	1.76 ± 0.44 [bc]	14.39	0.000[***]

Key: n = total number, SD = standard deviation, IL-6 = interleukin-6, CRP = c-reactive protein. *** Significant difference observed, p < 0.001. Different superscript letters (a, b, c) within the same row indicate statistically significant differences between groups based on post-hoc analysis (Tukey HSD).

Table 3: Mean DNA-Damage Biomarker Levels in Nonsmokers and Smokers in the Study Population at Baseline

Parameter	Mean ± SD					*F-value*	*p-value*
	Non-smokers (n = 30)	Shisha smokers (n = 30)	Cigarette smokers (n = 30)	Both Smokers (n = 30)	Second hand smokers (n = 30)		
$8NO_2$-Gua (ng/mL)	28.82 ± 4.82 [a]	30.40 ± 2.93 [a]	31.10 ± 3.29 [a]	30.65 ± 1.99 [a]	30.75 ± 3.91 [a]	1.25	0.294
4-HNE (ng/mL)	31.54 ± 3.46 [a]	32.08 ± 3.12 [a]	32.86 ± 2.82 [a]	31.89 ± 1.64 [a]	32.63 ± 2.61 [a]	0.75	0.562
MDA (µmol/L)	2.10 ± 0.68 [a]	2.72 ± 1.31 [a]	3.79 ± 2.30 [a]	3.99 ± 2.40 [a]	3.67 ± 2.73	4.08	0.176

Key: Same superscript letter ([a]) within a row indicates no statistically significant difference between groups based on post-hoc analysis; n = total number, SD = standard deviation, *F* = ANOVA statistic, p = error probability, $8NO_2$Gua = 8-Nitroguanine, 4-HNE = 4-hydroxynonenal and Malondialdehyde (MDA).

Table 4: Mean DNA-Damage Biomarker Levels in Nonsmokers and Smokers in the Study Population at Six Months Smoking

Parameter	Mean ± SD					*F-value*	*p-value*
	Non-smokers (n = 30)	Shisha smokers (n = 30)	Cigarette smokers (n = 30)	Both Smokers (n = 30)	Second hand smokers (n = 30)		
$8NO_2$-Gua (ng/mL)	28.82 ± 4.82 [a]	30.50 ± 2.06[ab]	31.31 ± 3.25[b]	31.43 ± 2.84 [b]	31.80 ± 2.88 [b]	2.60	0.041*
4-HNE (ng/mL)	31.54 ± 3.46 [a]	32.55 ± 2.50 [a]	33.17 ± 2.78 [a]	32.69 ± 2.76 [a]	32.63 ± 2.61[a]	0.92	0.456
MDA (µmol/L)	2.23 ± 0.99	2.91 ± 1.32 [ab]	3.97 ± 2.33 [b]	5.90 ± 3.10 [c]	3.90 ± 2.83 [b]	4.08	0.010[*]

Key: Statistical significance was determined by one-way ANOVA using multiple comparison with Tukey's post hoc analysis for comparison between the different groups. *P<0.05, n = total number, SD = standard deviation, *F* = ANOVA statistic, p = error probability, $8NO_2$Gua = 8-Nitroguanine, 4-HNE = 4-hydroxynonenal and Malondialdehyde (MDA). Different superscript letters (a, b, c) within the same row indicate statistically significant differences between groups based on post-hoc analysis (Tukey HSD).

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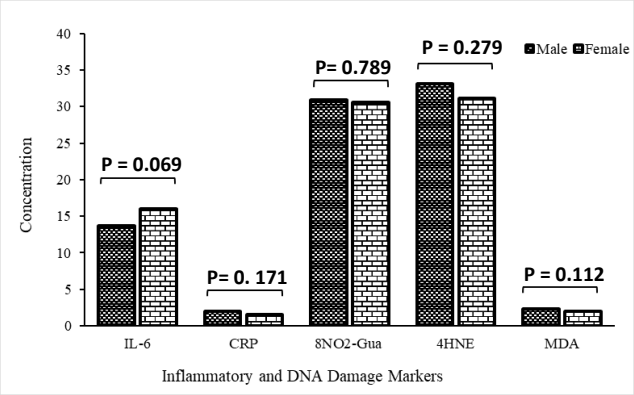

Figure 1: Mean levels of IL-6, CRP, $8NO_2$-Gua, 4-HNE and MDA in Shisha Smokers with Respect to Gender. $8NO_2$Gua = 8-Nitroguanine, 4-HNE = 4-hydroxynonenal and Malondialdehyde (MDA)

DISCUSSION

Tobacco use remains the leading global public health challenge, accounting for millions of deaths annually [23]. Shisha smoking exposes users to elevated concentrations of harmful chemicals, including polycyclic aromatic hydrocarbons, carbon monoxide, volatile organic compounds, particulate matter, and toxic metals such as aluminum, copper, manganese, cadmium, lead, arsenic, nickel, zinc, and cobalt. These substances contribute to the development of numerous medical conditions, including malignancies, chronic respiratory diseases, cardiovascular complications, and reproductive disorders [24].

Exposure to tobacco smoke has been linked to increased oxidative stress, potentially leading to vascular inflammation. Systemic inflammation and oxidative stress play a crucial role in respiratory and cardiovascular disorders [25]. Recent research has focused on inflammatory biomarkers in tobacco users, exploring the potential connection between smoking and the onset of inflammatory pathways [7,26]. However, some of these studies provided contradicting reports. C-reactive protein (CRP), a key marker of systemic inflammation, is an acute-phase protein produced primarily by the liver and adipose tissue under inflammatory conditions [11]. The inflammatory response leads to an elevated production of proinflammatory cytokines such as IL-6 and TNF-α from polymorphonuclear neutrophils, which then attach to their receptors on the surface of hepatocytes, stimulating further C-reactive protein synthesis [27].

In this study, serum IL-6 and CRP concentrations were significantly higher in shisha smokers, cigarette smokers, and both smokers and secondhand smokers compared with the non-smokers. Elevated CRP and IL-6 concentrations could be explained by inflammation triggered by tobacco smoke through the activation of signaling cascades such as mitogen-activated protein kinase (MAPK) and nuclear factor-κB (NF-κB), leading to increased production of various pro-inflammatory cytokines and chemokines [28]. Alternatively, exposure to tobacco smoke may lead to increased infiltration of macrophages, lymphocytes, and neutrophils in bronchoalveolar lavage fluid, accompanied by altered concentrations of several pro-inflammatory cytokines, including TNF-α, IL-1β, IL-6, IL-12, and IL-13 [29]. The findings are concurred with previous studies by Javed et al. [30] and Mokeem et al. [31], which reported an increased IL-6 level in shisha and e-cigarette users compared with non-smokers. Eworo et al. [32] and Jahan and Akhter [33] also indicated elevated levels of C-RP in smokers than non-smokers. Hartmann et al. [34] and Aneela et al. [35] also documented elevated levels of IL-6 in cigarette smokers compared to non-smokers. Ingrid et al. [36] also indicated a significant elevation of CRP and IL-6 levels in smokers compared to non-smokers.

The study also revealed that serum IL-6 and CRP levels in the shisha smokers were significantly higher ($p < 0.05$) than in cigarette smokers. This could be due to the fact that shisha smokers are at greater exposure risk to toxicants and larger volumes of smoke, which may trigger an inflammatory response, hence increasing the levels of interleukins and C-reactive protein [37]. Serum levels of IL-6 and CRP are slightly higher in the secondhand smokers than the waterpipe smokers, but not statistically significant ($p>0.05$). Serum IL-6 and CRP levels were significantly higher ($p<0.05$) in both (dual) smokers than shisha smokers. These findings indicate that the combined use of shisha and cigarettes may represent a significant risk factor for the development of chronic respiratory and cardiovascular disorders. This observation aligns with the report by Khabour et al. [29], which documented elevated IL-6 levels among waterpipe smokers.

Previous studies have evaluated gender-specific differences in smoking and IL-6 and CRP levels, reporting conflicting results [7, 38]. In this study, no significant

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difference was observed, but the serum IL-6 and CRP levels were slightly higher in the male smokers compared to the female smokers. Aldaham et al. [7] demonstrated that CRP levels did not differ significantly between genders in shisha smokers, but IL-6 levels were observed to be slightly decreased in females compared to males.

Tobacco smoking is reported to be associated with mutations in the p53 tumor suppressor gene, a critical change that results in uncontrolled cell proliferation, which is found in more than half of all human cancers [12]. Shisha smoke contains many deleterious chemicals such as nicotine, polycyclic aromatic hydrocarbon, 3-bromooctane, carbon monoxide, benzaldehyde, lead, zinc, cadmium, 1-methylcycloheptene, and tar [39], which raises the amount of free radicals in the body of smokers and can cause oxidative DNA damage, including single-strand breaks, apurinic/apyrimidic lesion formation, base modification, and chromosomal damage, thereby contributing to cancer development and a variety of genetic mutations [40]. 4-Hydroxynonenal is a highly reactive and diffusible byproduct of lipid peroxidation that plays a significant role in oxidative stress-mediated cellular signaling and programmed cell death (apoptosis) [41]. 8-Nitroguanine is formed through the interaction between guanine in DNA and reactive nitrogen species (RNS), particularly peroxynitrite ($ONOO^-$). Both 4-HNE and 8-NO_2-Gua serve as specific indicators of DNA damage resulting from oxidative and nitrosative stress, and they are closely linked to mutagenesis, cancer development, and persistent inflammatory diseases.

In this study, serum 8-NO_2-Gua and MDA levels were significantly higher ($p<0.05$) in shisha smokers, cigarette smokers, both smokers, and secondhand smokers compared with the non-smokers. Serum 4-HNE levels were slightly higher in all categories of smokers compared with the nonsmokers. This elevation could be attributed to the fact that tobacco smoke generates reactive oxygen species (ROS) that attack polyunsaturated fatty acids in cell membranes, leading to the formation of 4-HNE, or due to the fact that tobacco smoke releases reactive nitrogen species (RNS), such as peroxynitrite, which react with guanine in DNA to form 8-NO_2-Gua, leading to a rise in 8-NO_2-Gua. Yadav and Thakur [42] indicated that shisha smoke was linked to an elevation in frequency of chromosomal aberrations (CA), sister chromatid exchanges (SCE), and mitotic index in waterpipe smokers compared with non-smokers. Serum 8NO_2^--Gua, 4-HNE, and MDA levels in shisha smokers were slightly higher than in cigarette smokers. Also, a slight elevation ($p > 0.05$) was observed for 8-NO_2-Gua, 4-HNE, and MDA levels in secondhand smokers compared to shisha smokers. Both smokers exhibited significantly higher 8-NO_2-Gua and MDA levels compared to the exclusive shisha smokers. This is in accordance with the previous study by Khan et al. [43]. Previous clinical studies by Alsatari et al. [44] and Khabour et al. [45] indicated that shisha smoking is genotoxic, and the degree of its genotoxicity was greater than that induced by cigarette smoking. Bayoumi and Co-workers [46] indicated an increase in chromosomal breaks, chromosomal terminal deletions, and polyploidy among the tobacco smoker groups. However, no significant difference was observed between the smoker groups, which is similar to the findings of this study. There was no specific gender difference observed in serum 8-NO_2-Gua, 4-HNE, and MDA levels, but a slight increase was observed in male smokers compared to the female smokers.

CONCLUSION

The study revealed that systemic inflammatory (IL-6 and CRP), oxidative stress (MDA), and DNA damage markers (8-NO_2-Gua, 4-HNE) were significantly elevated in shisha smokers and cigarette smokers. It further confirmed that concurrent smoking of shisha and cigarettes exerts more deleterious effects than exclusive shisha or cigarette smoking, aggravating pulmonary and cardiovascular conditions. Results obtained from this study provide valuable evidence to inform both the public and policymakers about the health risks associated with shisha and cigarette smoking, emphasizing the need for increased public awareness campaigns.

Limitations

The study has a limited sample size due to financial or sampling constraints, which may not fully represent all shisha smokers in Yenagoa City. A larger sample size would have provided more precise values and enhanced the reliability of the observed trends. In addition, there is the possibility of confounding exposures such as environmental pollution or local dietary habits, which

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might influence the concentration of the analyzed biomarkers.

Author's Contributions

Onitsha, Enebrayi Nelson is solely responsible for all aspects of the research. The author takes responsibility for the study's conception, design, data acquisition, analysis, and manuscript preparation.

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Conflict of Interest

The author declares there is no conflict of interest.

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