Air Concentrations of Nitrogen Oxide Related to Tobacco Smoke: A Systematic Review

Mobina Shamansouri1, Kosar Shahabi1, Roohollah Rostami2,1*

1Research Center for Health Sciences and Technologies, Semnan University of Medical Sciences, Semnan, Iran
2Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran

Abstract
Environmental tobacco smoke (ETS), similar to firsthand and secondhand smoke, is a complex mixture containing thousands of chemicals, many of which are known as carcinogens. The high combustion temperature of tobacco and the presence of nitrogen in the tobacco can lead to the release of nitrogen oxides (NOx). From the NOx, NO2 irritates the respiratory system and damages cells and mucous membranes of the lungs. The selected databases for this systematic review were Science Direct, Springer, PubMed, and Google Scholar, and the keywords of the search plan included “nitrogen oxide”, “NOx”, “ETS”, “Cigarette smoke”, “Waterpipe smoke”, and “Tobacco smoke”. Finally, 797 articles were found, and after reviewing, 7 articles met our criteria. The results demonstrated that the mean air concentration of tobacco smoke related-NOx was 9.71 ± 11.03 ppm, which was higher than the annual guideline level of free air quality (0.053 ppm). The mean concentration of NOx in cigarette smoke was 329.45 ± 465.43 ppm, and for smoking places, it was higher than for nonsmoking places (17.80 vs. 12.47 ppm). Moreover, for the cigarette smoke, it was higher than for the waterpipe smoke (5.66 vs. 0.16 ppm). In this regard, the cigarette is more suspected to the emission of NOx compared to waterpipe, and tobacco smoking can expose people to high levels of NOx regarding the limited guideline levels. Finally, the concentration of NO in cigarette smoke and air was higher than NO2.

Keywords: Air pollution, Cigarette, Waterpipe, Nitrogen oxides

Introduction
Numerous scientific documents show that tobacco use is associated with major threats to health. It is indicated that 440,000 people in the United States are threatened annually in this way, and the related healthcare cost is equivalent to 157 billion dollars per year (1). Environmental tobacco smoke (ETS) is similar to mainstream smoke inhaled by a smoker and is a complex mixture containing thousands of chemicals, many of which are carcinogens. There is convincing evidence from numerous experimental and epidemiological studies that secondhand smoke increases the incidence of lung cancer and cardiovascular disease and is also responsible for other severe health effects such as asthma. In this regard, ETS has been classified as a human carcinogen (1). It is stated that smoking is an important risk factor for cardiovascular diseases (2). Waterpipe consumption is an old method of smoking and spread out in recent years, especially in Arab and Middle Eastern societies (3). Although cigarette smoking is the most common in Iran, waterpipe smoking has recently increased among the youth (4). It is expanding among the community and there is insufficient information on the harmful effects of waterpipe use for nitrogen oxides (NOx) (5). The high temperature of the combustion of tobacco leads to the formation of NO and NO2. Road traffic is the main source of NO2 in the urban ambient air, and the most important indoor sources include tobacco smoke and the combustion of fuel, wood, and coal. Outdoor NO2 from natural and anthropogenic sources also affects indoor concentration. As NO2 exists mainly in the gaseous form, inhalation is the main route of its exposure (6). Regarding the effect of exposure to NOx on health and the relation between tobacco smoking and the emission of NOx, this study considered the concentration of NOx in the literature which was related to tobacco smoking and the influencing factors.

Methods
The present review study was performed from the 18th of December to the 11th of November 2022 on Science Direct, Springer, PubMed, and Google Scholar databases.
for English articles. The search keywords included “Nitrogen oxide”, “NO\textsubscript{2}”, “ETS”, “Cigarette smoke”, “Waterpipe smoke”, and “Tobacco smoke”. It resulted in 797 articles, including 19 subject-related cases. Next, reviewing the full articles, finally, 7 articles were selected to include in the study regarding the study criteria. The inclusion criterion was reporting the concentration of NOx in indoor environments related to tobacco smoking, while the exclusion criterion was the NOx not related to tobacco smoke.

**Results**

**Concentration of Nitrogen Oxide in Indoor Air**
The results revealed that the mean concentration of NO\textsubscript{x} in the indoor air was 9.71 ± 11.03 ppm, which was higher than the annual guideline level of ambient air quality (0.053 ppm) (1, 7-13). In indoor environments, the maximum and minimum concentrations of NO\textsubscript{x} were 24.70 and 0.15 ppm, respectively. Both of them were higher than the guideline limit (0.053 ppm) (1, 7-13). For instance, Freeman et al declared that the annual emission of NO\textsubscript{x} from waterpipe smoking in Kuwait was 744.30 kg (14). Given the results, the concentration of NO and NO\textsubscript{2} in the indoor air was 0.1 ppm and 0.06 ppm (Figure 1).

**Concentration of Nitrogen Oxides in Cigarette Smoke**
The results represented that the mean concentration of NO\textsubscript{x} in cigarette smoke was 329.45 ± 465.43 ppm, which is higher than the annual guideline level of ambient air quality (0.053 ppm) (1, 7-13). The maximum and minimum concentrations of NO\textsubscript{x} were 658.57 and 0.34 ppm, and both of them were higher than the guideline limit (0.053 ppm) (1, 7-13). According to the result, the mean concentration of NO and NO\textsubscript{2} were 0.23 and 0.10 ppm, respectively. Both of them were higher than the guideline limit (0.053 ppm) (1, 7-13). Rickert et al reported that the emitted NO by the smoke of 15 types of cigarettes was 1.44 µmol/cigarette. They concluded that it was about 13% of the mean reported for American cigarettes (12). Mannix found the highest concentration of NOx from cigarette smoke up to 2.27 ± 0.57 mg/m\textsuperscript{3} (15). According to the results, the concentration of NO in cigarette smoke was higher than that of NO\textsubscript{2} in the smoke (Figure 2).

**Concentration of Nitrogen Oxide in Waterpipe Smoking and Nonsmoking Places**
The results showed that the mean concentration of NO\textsubscript{x} in smoking and nonsmoking places was 17.80 and 12.47 ± 17.29 ppm, respectively (1, 7-13). Ghasemi et al reported that the serum level of NO\textsubscript{x} for active smokers (28.2 ± 1.0 µmol/L) was higher than for passive smokers and non-smokers (25.3 ± 1.0 µmol/L) (16). According to the results, the mean concentration of NO\textsubscript{x} in smoking places was higher than that in nonsmoking places (Figure 3).

**Concentration of Nitrogen Oxide in Waterpipe Smoke and Cigarette Smoke**
The results showed that the mean concentration of NO\textsubscript{x} in tobacco smoke was 10.72 ± 12.47 ppm, which is higher than the annual guideline level of ambient air quality (0.053 ppm) (1, 7-13). The mean concentration of NO\textsubscript{x} in cigarette and waterpipe side streams were 5.66 and 0.16 ppm, respectively (1, 7-13). Both of them were high compared to the annual guideline limit (0.053 ppm). About the workplaces, the time-weighted average and short-term exposure limits for NO\textsubscript{x} are 3
and 5 ppm, respectively (17). They were higher than the concentrations of NOx for the tobacco smoke of cigarette and waterpipe's side streams. Based on the results, the concentration of NOx in cigarette smoke was higher than that for the waterpipe smoke (Figure 4).

Discussion
According to the results, the mean concentration of NOx in the smoking places was higher than in nonsmoking places. Braun et al reported substantial increases in NOx concentration when smoking only one cigarette as the NOx mean concentrations ranged between 105 and 293 µg/m³, and the maximum concentration was 357 µg/m³ (8). Notable emission of NOx was reported from tobacco smoking, and the concentration of NO was higher than of NO2 in the indoor air related to tobacco smoke. Middleton et al found that NOx is mainly in the form of NO in the exhaust of combustion units and then it turns into NO2 (18). It can be implied that the higher concentration of NO compared to NO2, is due to the proximity of the combustion source of NOx in the smoking environments.

The result demonstrated that the mean concentration of NOx in cigarette smoke was higher than the guideline limit for ambient air quality. Previous research confirmed that the lighted cigarette is a source of notable concentration of NOx, and it is increased with a warm-up of the light as the concentrations of 146, 204, and 213 ppm were found at 10, 20, and 37 seconds after the lightening of cigarette, respectively, and they were also drastically higher than the exposure limit (19). In this way, the highest mean concentration of NOx was found in cigarette smoke (658.57 ppm), while the lowest one was observed in waterpipe smoke (0.16 ppm) (1, 7-13). The high concentration of NOx in cigarette smoke was also reported by Cvetkovic et al (20).

Based on the results, the mean concentration of NOx in tobacco smoke was 10.72 ± 12.47 ppm, which was higher than the annual guideline level of ambient air quality (0.053 ppm). Anyanwu et al concluded that NO can act as a vasodilator of cerebral blood vessels, causing cytotoxic activities in the immune system, as well as acting as a neurotransmitter (21). Krzeszowiak et al found that NOx can further react in the bloodstream as it is a water-based environment. Highly reactive NOx generates superoxide and alkoxy radicals, and the ensuing nitrogen anion imbalance contributes to lipid peroxidation (22). Tobacco smoke is one of the sources of NO and NOx, which are increasingly implicated in a wide range of disorders. For example, the increased risk of otitis media, eczema ear/nose/throat infections, and sensitization to food allergens in children, as well as increased blood coagulability after periods of elevated ambient exposure in adults have been reported recently (23).

Conclusion
The results revealed that the concentration of NOx in cigarette smoke is higher than that of waterpipe smoke. According to the results, the concentration of NOx in smoking places was higher than in nonsmoking places. Additionally, in the air and in cigarette smoke, the concentration of NO was higher than that of NO2. Considering the total nitrogen oxide in the form of NOx in cigarette smoke and waterpipe smoke, its concentration was higher than the annual guideline of outdoor air quality; however, they were lower compared to the guideline limits for workplaces. Indoor exposure to the NOx from tobacco smoke can lead to adverse health effects and thus needs further consideration.

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Authors’ Contribution
Conceptualization: Roohollah Rostami.
Data curation: Kosar Shahabi, Mobina Shamansouri.
Formal analysis: Kosar Shahabi, Mobina Shamansouri.
Funding acquisition: Roohollah Rostami.
Investigation: Roohollah Rostami.
Methodology: Roohollah Rostami.
Project administration: Kosar Shahabi, Mobina Shamansouri.
Supervision: Roohollah Rostami.
Validation: Roohollah Rostami.
Visualization: Kosar Shahabi, Mobina Shamansouri.
Resources: Kosar Shahabi, Mobina Shamansouri, Roohollah Rostami.
Writing—original draft: Kosar Shahabi, Mobina Shamansouri.
Writing—review & editing: Roohollah Rostami.

Competing Interests
The authors certify that they have no affiliation with or financial interest in the subject matter or materials discussed in this research.

Ethical Approval
Not applicable.
References


