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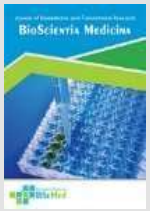

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Analysis of Risk Factors and The Impact of Nitric Oxide (NO) and Carbon Monoxide (CO) Levels on Lung Function: A Comparative Study of Palm Oil Factory Workers and the Community in Kuantan Mudik District, Riau, Indonesia

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A B S T R A C T

Background: Air pollution, particularly from industrial sources like palm oil factories, poses a significant risk to respiratory health. This study aimed to investigate the impact of nitric oxide (NO) and carbon monoxide (CO) exposure on lung function in palm oil factory workers and compare it to the lung function of individuals in the surrounding community. **Methods:** A cross-sectional study was conducted in Kuantan Mudik District, Riau, Indonesia. One hundred palm oil factory workers with a minimum of two years of employment and 100 community members not occupationally exposed to NO and CO were recruited. Lung function was assessed using spirometry, and NO and CO levels were measured using specialized analyzers. Participants completed the European Community Respiratory Health Survey (ECRHS) questionnaire, and demographic and clinical data were collected. Statistical analyses included univariate, bivariate, and multivariate logistic regression. **Results:** Factory workers exhibited significantly higher levels of NO (p=0.000) and a higher prevalence of restrictive lung function (17%) compared to the community members (3%). Multivariate analysis identified NO exposure as the most significant risk factor for restrictive lung function (p=0.005). Each unit increase in NO was associated with a 1.12-fold increased risk of restrictive lung function. CO exposure, age, gender, smoking history, and the use of personal protective equipment (PPE) were not significantly associated with lung function impairment in this study. **Conclusion:** Occupational exposure to NO in palm oil factories is a significant risk factor for restrictive lung function impairment. Regular monitoring of NO levels and the implementation of effective control measures are crucial to protect the respiratory health of palm oil factory workers.

1. Introduction

Air quality is a critical determinant of human health, and its degradation due to pollution poses a significant global challenge. The World Health Organization (WHO) estimates that a staggering 91% of the world's population breathes air that fails to meet its quality standards. This alarming statistic underscores the urgency of addressing air pollution and its detrimental impacts on human health, particularly within the respiratory system. Industrial activities are major contributors to air pollution, releasing a cocktail of harmful substances into the atmosphere. Among these pollutants, nitric oxide (NO) and carbon monoxide (CO) are of particular concern due to their well-documented adverse effects on respiratory health. NO, a free radical gas, is a byproduct of combustion processes and can trigger airway inflammation and oxidative stress, compromising lung function. CO, another toxic gas produced by incomplete combustion, binds to hemoglobin, reducing the blood's oxygen-carrying capacity and potentially leading to hypoxia. The palm

oil industry, a cornerstone of the Indonesian economy, is a significant source of air pollution. Indonesia is the world's leading producer of palm oil, with vast plantations and numerous processing factories scattered across the country. While this industry plays a crucial role in economic development, it also raises concerns about its environmental and health impacts. Workers in palm oil factories are chronically exposed to a complex mixture of air pollutants, including NO and CO, due to the nature of their work, which often involves close proximity to combustion sources.[1-3]

The respiratory health consequences of air pollution exposure have been extensively studied in various occupational and environmental settings. Research on traffic police officers, parking attendants, and individuals residing near major roadways has consistently linked exposure to traffic-related air pollution with reduced lung function and increased respiratory symptoms. These studies highlight the vulnerability of individuals exposed to air pollution, particularly those in occupations that entail prolonged or intense exposure. In the context of palm oil factories, workers are potentially at heightened risk due to the nature of the production process, which involves activities such as the burning of biomass and the operation of diesel engines. These processes release significant amounts of NO and CO into the workplace environment, increasing the likelihood of inhalation and subsequent adverse health effects. While the detrimental effects of air pollution on respiratory health are well-established, there remains a gap in our understanding of the specific impact of NO and CO exposure on lung function in palm oil factory workers. This knowledge gap is particularly relevant in Indonesia, where the palm oil industry is a major employer and contributor to the national economy. To address this gap, our study aimed to investigate the relationship between NO and CO exposure and lung function in palm oil factory workers. We conducted a cross-sectional study comparing the lung function of palm oil factory workers to that of individuals in the surrounding community who were not occupationally exposed to these pollutants. By examining the levels of NO and CO in both groups and assessing their lung function using spirometry, we sought to determine whether occupational exposure to these pollutants was associated with impaired lung function.[4-6] Furthermore, we aimed to identify other risk factors that might contribute to lung function impairment in this population. These risk factors included demographic factors (age, gender), lifestyle factors (smoking history), and occupational factors (duration of employment, and use of personal protective equipment). By analyzing the interplay of these factors, we hoped to gain a comprehensive understanding of the determinants of respiratory health in palm oil factory workers. Our study is the first to specifically investigate the impact of NO and CO exposure on lung function in palm oil factory workers in Indonesia. The findings of this study have important implications for occupational health and safety in the palm oil industry. By identifying the risk factors associated with impaired lung function, we can inform the development of targeted interventions to protect the respiratory health of palm oil factory workers. These interventions may include measures to reduce NO and CO emissions, the provision of personal protective equipment, and health education programs to raise awareness about the risks of air pollution exposure.

2. Methods

This cross-sectional study was conducted at a palm oil factory (PT.X) located in Kuantan Mudik District, Kuantan Singingi Regency, Riau Province, Indonesia. The study period spanned from August 2023 to November 2023. The palm oil factory was chosen due to its potential for high occupational exposure to air pollutants, including nitric oxide (NO) and carbon monoxide (CO), which are byproducts of the combustion processes involved in palm oil production. The surrounding community, Village X, was selected as a control group due to the assumption of minimal occupational exposure to these pollutants. A total of 100 workers from PT.X were recruited. These workers

were primarily involved in outdoor activities, such as boiler operation and production, where exposure to air pollutants is expected to be higher. To be eligible for inclusion, workers had to have been employed at the factory for a minimum of two years. This criterion was established to ensure that the workers had experienced a substantial duration of exposure to the factory's environmental conditions. A control group of 100 residents from Village X was also recruited. These individuals were assumed to have no occupational exposure to NO and CO, providing a baseline for comparison with the factory workers. To ensure the validity and reliability of the study findings, specific inclusion and exclusion criteria were applied. Inclusion Criteria: Factory Workers: Employed at PT.X for at least two years; Willingness to participate in the study, including signing an informed consent form, completing questionnaires, and undergoing spirometry and pollutant level testing. Community Members: Residents of Village X; No occupational exposure to NO and CO; Willingness to participate in the study, including signing an informed consent form, completing questionnaires, and undergoing spirometry and pollutant level testing. Exclusion Criteria: Individuals with pre-existing respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), or other chronic lung conditions. These individuals were excluded to avoid confounding the results, as their lung function may be impaired due to their underlying conditions rather than exposure to air pollutants.

A comprehensive data collection approach was employed to gather relevant information from the participants. All participants completed the European Community Respiratory Health Survey (ECRHS) questionnaire. This standardized questionnaire is widely used in respiratory research and collects data on respiratory symptoms (e.g., cough, wheezing, shortness of breath), smoking history, occupational history, and other potential confounding factors. The questionnaire was administered in the local language (Indonesian) to ensure comprehension and accurate responses. Spirometry, a well-established pulmonary function test, was used to assess lung function in all participants. This non-invasive test measures the volume and flow of air that can be inhaled and exhaled. Key spirometry parameters recorded included: Forced Vital Capacity (FVC): The maximum volume of air that can be exhaled forcefully after a deep inhalation; Forced Expiratory Volume in One Second (FEV1): The volume of air exhaled in the first second of a forced exhalation; FEV1/FVC Ratio: The proportion of the FVC exhaled in the first second. This ratio is a crucial indicator of airway obstruction. Spirometry tests were conducted by trained technicians following standardized protocols to ensure consistency and accuracy. Exhaled breath samples were collected from all participants to measure NO and CO levels. These measurements were performed using specialized analyzers: NO Analyzer: This device measures the concentration of nitric oxide in exhaled breath. NO is a marker of airway inflammation and can be elevated in various respiratory conditions; CO Analyzer: This device measures the concentration of carbon monoxide in exhaled breath. CO is a toxic gas that can bind to hemoglobin, reducing oxygen-carrying capacity. The analyzers used in this study were calibrated and validated to ensure accurate and reliable measurements.

In addition to the questionnaire and spirometry data, demographic and clinical information was collected from all participants. This included: Age: Recorded in years; Gender: Male or female; Body Mass Index (BMI): Calculated as weight (kg) divided by height squared (m^2). BMI is a measure of body fat and can be used to assess nutritional status; Smoking History: Detailed information on smoking habits, including the number of cigarettes smoked per day, duration of smoking, and smoking status (current smoker, former smoker, or never smoker); Occupational History: Information on the type of work performed, duration of employment, and use of personal protective equipment (PPE) in the workplace; Medical History: Any history of respiratory or other relevant medical conditions. The collected data were analyzed using statistical software (SPSS version 26).

The analysis involved several steps: Descriptive statistics were used to summarize the characteristics of the study population. This included calculating means, standard deviations, medians, and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables; Univariate analysis was performed to describe the distribution and frequency of each variable. This helped to identify any outliers or unusual patterns in the data; Bivariate analysis was conducted to examine the relationship between lung function (FEV1/FVC) and exposure to CO and NO. The chi-square test was used for categorical variables, and the Mann-Whitney U test was used for continuous variables; Multivariate logistic regression analysis was performed to identify independent risk factors for impaired lung function. This analysis allowed us to control for potential confounding factors and determine the specific contribution of each variable to the risk of impaired lung function. The study protocol was approved by the Institutional Ethics Committee of the Faculty of Medicine, University of Riau. All participants provided written informed consent before enrollment. The study adhered to the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Confidentiality and anonymity of the participants were maintained throughout the study.

3. Results

Table 1 presents the demographic and clinical characteristics of the study participants, comparing palm oil factory workers (n=100) to community members (n=100). The average age of factory workers was slightly higher than that of community members (39 years vs. 36 years), although this difference was not statistically significant (p=0.52). There was a significant difference in gender distribution between the two groups (p=0.00), with a higher proportion of males in the factory worker group (97%) compared to the community member group (51%). The prevalence of abnormal CO levels was higher in factory workers (18%) than in community members (2%), but this difference was not statistically significant (p=0.09). However, abnormal NO levels were exclusively observed in factory workers (31%), indicating a significant difference between the two groups (p=0.00). The prevalence of restrictive lung function, a measure of impaired lung function, was also significantly higher in factory workers (17%) compared to community members (3%) (p=0.01).

Table 1. Participant characteristics.

Characteristic	Factory workers (n=100)	Community members (n=100)	p-value
Age (years), mean (SD)	39 (13)	36 (13)	0.52
Gender, n (%)			
Male	97 (97%)	51 (51%)	0.00*
Female	3 (3%)	49 (49%)	
Abnormal CO levels, n (%)	18 (18%)	2 (2%)	0.09
Abnormal NO levels, n (%)	31 (31%)	0 (0%)	0.00*
Restrictive lung function, n (%)	17 (17%)	3 (3%)	0.01*

Table 2 displays the lung function parameters (FVC, FEV1, FEV1/FVC) and pollutant levels (NO, CO) in palm oil factory workers and community members. Factory workers exhibited slightly lower mean values for FVC (3.21 L vs. 3.38 L) and FEV1 (2.85 L vs. 2.97 L) compared to community members, although these differences were not statistically significant (p=0.06 and p=0.11, respectively). The FEV1/FVC ratio, a key indicator of airway obstruction, was also similar between the two groups (88.9% vs. 89.5%, p=0.53). In contrast, NO levels were significantly higher in factory workers (median 21 ppb) compared to community members (median 12 ppb) (p=0.00). This finding suggests that factory workers are exposed to higher levels of NO, which is a concerning observation given the potential for NO to cause airway inflammation and

respiratory problems. CO levels were also higher in factory workers (median 7 ppm) compared to community members (median 4 ppm), but this difference was not statistically significant (p=0.09).

Table 2. Lung function and pollutant levels.

Parameter	Factory workers (n=100)	Community members (n=100)	p-value
FVC (L), mean (SD)	3.21 (0.54)	3.38 (0.62)	0.06
FEV1 (L), mean (SD)	2.85 (0.48)	2.97 (0.55)	0.11
FEV1/FVC (%), mean (SD)	88.9 (6.2)	89.5 (5.8)	0.53
NO (ppb), median (IQR)	21 (11)	12 (8)	0.00*
CO (ppm), median (IQR)	7 (8)	4 (9)	0.09

Table 3 presents the results of both bivariate and multivariate analyses examining the risk factors associated with restrictive lung function in palm oil factory workers and community members. In the bivariate analysis, nitric oxide (NO) levels, duration of employment, and smoking history were all significantly associated with restrictive lung function ($p<0.05$). This suggests that higher NO levels, longer employment duration, and a history of smoking may increase the risk of developing restrictive lung function. However, in the multivariate analysis, which adjusts for the effects of other variables, only NO levels remained a significant predictor of restrictive lung function (p=0.005). The odds ratio of 1.12 (95% CI 1.05-1.20) indicates that for each unit increase in NO levels, the risk of restrictive lung function increases by 12%. This suggests that NO exposure is an independent risk factor for restrictive lung function, regardless of other factors such as duration of employment or smoking history. The duration of employment and smoking history, while significant in the bivariate analysis, were not significant predictors in the multivariate analysis. This suggests that their association with restrictive lung function may be explained by their relationship with NO levels or other unmeasured factors.

Table 3. Bivariate and multivariate analysis of risk factors for restrictive lung function.

Risk factor	Bivariate analysis	Multivariate analysis
	p-value	Odds Ratio (95% CI)
NO (ppb), per unit increase	0.000*	1.12 (1.05-1.20)#
Duration of employment (years)	0.001*	1.03 (0.98-1.08)
Smoking history (pack-years)	0.004*	1.01 (0.99-1.03)

*Bivariate analysis, p<0,05; #Multivariate analysis, p<0,05.

4. Discussion

The significantly higher prevalence of restrictive lung function (17%) observed in palm oil factory workers compared to community members (3%) in this study strongly emphasizes the potential occupational hazard posed by nitric oxide (NO) exposure in this industry. Restrictive lung function, a condition characterized by reduced lung volumes and capacities, can manifest as debilitating symptoms such as shortness of breath, chest tightness, and decreased exercise tolerance, severely impacting the quality of life of affected individuals. The long-term consequences of this condition can be dire, potentially leading to respiratory failure and increased mortality rates. The mechanisms through which NO exposure contributes to lung function impairment are indeed complex and multifaceted, encompassing both direct and indirect pathways. NO, a highly reactive free radical gas, can initiate a cascade of detrimental effects within the respiratory system. One of the primary mechanisms is

the induction of oxidative stress, a state of imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses. NO can directly react with oxygen molecules to generate ROS, such as superoxide radicals and peroxynitrite, which can overwhelm the antioxidant system and cause damage to cellular components, including lipids, proteins, and DNA. This oxidative damage can disrupt normal cellular function, leading to impaired lung elasticity, reduced surfactant production, and ultimately, restrictive lung function.[7-10]

In addition to oxidative stress, NO can also trigger and perpetuate inflammatory responses within the airways and lung parenchyma. NO can activate various inflammatory cells, such as macrophages, neutrophils, and eosinophils, leading to the release of pro-inflammatory cytokines (e.g., TNF-alpha, IL-1beta, IL-6) and chemokines (e.g., IL-8). These inflammatory mediators can recruit additional immune cells to the lungs, amplifying the inflammatory response and causing further damage to lung tissue. Chronic inflammation can result in airway remodeling, characterized by structural changes such as airway smooth muscle hypertrophy, goblet cell hyperplasia, subepithelial fibrosis, and increased collagen deposition. These changes can significantly impair lung function by reducing airway caliber, increasing airway resistance, and decreasing lung compliance, all of which contribute to the development of restrictive lung disease. Furthermore, NO can also interact with other air pollutants, such as particulate matter (PM), to form more toxic compounds, such as nitrogen dioxide (NO_2) and peroxyacetyl nitrate (PAN). These secondary pollutants can further exacerbate respiratory inflammation and damage, leading to a vicious cycle of oxidative stress, inflammation, and lung function impairment. The effects of NO on lung function are not limited to the airways and lung parenchyma. NO can also affect the pulmonary vasculature, leading to vasoconstriction and increased pulmonary vascular resistance. This can result in pulmonary hypertension, a serious condition characterized by high blood pressure in the lungs, which can further impair lung function and lead to right heart failure.[11-13]

The complex interplay between NO, oxidative stress, inflammation, and other air pollutants creates a challenging environment for the respiratory system. The long-term consequences of chronic NO exposure can be severe, including the development of chronic respiratory diseases such as COPD, interstitial lung disease, and even lung cancer. Understanding the mechanisms through which NO contributes to lung function impairment is crucial for developing effective prevention and treatment strategies. Antioxidant therapies, anti-inflammatory drugs, and interventions targeting specific molecular pathways involved in NO-induced lung damage are potential avenues for future research. Additionally, reducing NO emissions from industrial sources, such as palm oil factories, and promoting the use of personal protective equipment can help to minimize occupational exposure and protect the respiratory health of workers. Particulate matter (PM) is a complex mixture of solid particles and liquid droplets suspended in the air. These particles vary in size, composition, and origin, and their health effects depend on these characteristics. Fine particulate matter (PM2.5), with an aerodynamic diameter of 2.5 micrometers or less, is of particular concern due to its ability to penetrate deep into the respiratory system, reaching the alveoli. NO can react with PM2.5 in the atmosphere to form NO_2, a potent respiratory irritant. NO_2 can cause bronchoconstriction, airway hyperresponsiveness, and inflammation, leading to reduced lung function. Studies have shown that exposure to NO_2 is associated with increased respiratory symptoms, decreased lung function, and exacerbation of asthma and COPD. In addition to NO_2, the interaction of NO with PM2.5 can also lead to the formation of PAN. PAN is a secondary pollutant formed from the reaction of NO_2 with volatile organic compounds (VOCs) in the presence of sunlight. PAN is a strong respiratory irritant and can cause eye irritation, coughing, and difficulty breathing. Studies have linked PAN exposure to decreased lung function and increased respiratory

symptoms in both healthy individuals and those with pre-existing respiratory conditions.[13-16]

The combined effects of NO, NO_2, and PAN on respiratory health create a synergistic effect, where the toxicity of these pollutants is amplified when they are present together. This synergistic effect can lead to more severe respiratory inflammation and damage, resulting in greater lung function impairment than would be expected from exposure to each pollutant individually. Both NO and PM2.5 can generate reactive oxygen species (ROS), which are highly reactive molecules that can damage cellular components, including lipids, proteins, and DNA. The combined generation of ROS from NO and PM2.5 can overwhelm the antioxidant defenses of the respiratory system, leading to increased oxidative stress and cellular damage. NO and PM2.5 can both trigger inflammatory responses in the respiratory system. NO can activate inflammatory cells, such as macrophages and neutrophils, leading to the release of pro-inflammatory cytokines and chemokines. PM2.5 can also activate inflammatory cells and induce the production of inflammatory mediators. The combined inflammatory response to NO and PM2.5 can result in more severe airway inflammation and damage. The mucociliary escalator is a defense mechanism of the respiratory system that helps to remove inhaled particles and pathogens. NO and PM2.5 can both impair mucociliary clearance by damaging ciliated cells, reducing mucus production, and altering the rheological properties of mucus. The combined impairment of mucociliary clearance can lead to the accumulation of pollutants and pathogens in the airways, further exacerbating respiratory inflammation and damage.[16,17]

The synergistic effects of NO and PM2.5 have significant implications for the respiratory health of palm oil factory workers. These workers are exposed to a complex mixture of air pollutants, including both NO and PM2.5, which are generated from various sources within the factory environment. The combined exposure to these pollutants can increase the risk of developing respiratory problems, such as asthma, COPD, and restrictive lung function. The findings of our study, which showed a significant association between NO exposure and restrictive lung function impairment in palm oil factory workers, highlight the importance of considering the synergistic effects of air pollutants when assessing occupational health risks. It is crucial to monitor and control the levels of both NO and PM2.5 in palm oil factories to protect the respiratory health of workers. The most effective way to reduce the health risks associated with air pollution is to reduce emissions at the source. This can be achieved through the use of cleaner technologies, such as low-NOx burners and electrostatic precipitators, which can significantly reduce NO and PM2.5 emissions from industrial processes. Proper ventilation systems can help to dilute and remove air pollutants from the workplace environment. This can be achieved through the use of exhaust fans, air filters, and other ventilation technologies. Workers should be provided with appropriate Personal Protective Equipment (PPE), such as respirators, to protect their respiratory system from exposure to air pollutants. The type of respirator required will depend on the specific pollutants present and their concentrations. Regular health monitoring of workers can help to identify early signs of respiratory problems and allow for timely intervention. This can include spirometry testing, chest X-rays, and other diagnostic tests.[17,18]

Further research is needed to fully understand the complex interactions between NO and other air pollutants, such as PM2.5, and their combined effects on respiratory health. Longitudinal studies are needed to investigate the long-term effects of exposure to these pollutants and to identify susceptible populations. Additionally, research should focus on developing and evaluating effective interventions to reduce exposure and mitigate the health risks associated with air pollution in occupational settings. The findings of this study have significant implications for the palm oil industry and occupational health. The high prevalence of restrictive lung function in palm oil factory workers suggests that current occupational health and safety measures may not be sufficient to protect workers

from the harmful effects of NO exposure. This highlights the need for stricter regulations and monitoring of air quality in palm oil factories, as well as the implementation of effective control measures to reduce NO emissions. Furthermore, the study emphasizes the importance of raising awareness among palm oil factory workers about the potential health risks associated with NO exposure. Workers should be educated about the importance of using personal protective equipment (PPE), such as masks, to minimize their exposure to NO and other air pollutants. Regular health checkups, including lung function tests, should also be conducted to monitor the respiratory health of workers and identify early signs of lung function impairment. In addition to occupational health interventions, efforts should also be made to reduce NO emissions from palm oil factories at the source. This can be achieved through the adoption of cleaner production technologies, such as using low-NOx burners in boilers and implementing efficient emission control systems. Investing in research and development of sustainable and environmentally friendly palm oil production practices can also contribute to reducing air pollution and protecting the health of both workers and the surrounding communities. The findings of this study also have broader implications for public health. The palm oil industry is a major contributor to air pollution in many regions, and the release of NO and other pollutants from palm oil factories can have adverse health effects on nearby communities. Therefore, it is crucial to consider the environmental and health impacts of palm oil production and to promote sustainable practices that minimize air pollution and protect public health. The observed higher prevalence of restrictive lung function in palm oil factory workers compared to community members underscores the potential occupational hazard posed by NO exposure in this industry. The multifaceted mechanisms underlying NO-induced lung function impairment, including oxidative stress, inflammation, and interactions with other air pollutants, highlight the complex nature of this issue. Addressing this occupational health hazard requires a multi-pronged approach, including stricter regulations, improved monitoring, effective control measures, worker education, and the adoption of cleaner production technologies. By prioritizing the health and well-being of palm oil factory workers and the surrounding communities, we can strive toward a more sustainable and equitable palm oil industry.[19,20]

5. Conclusion

Our study provides evidence that occupational exposure to NO in palm oil factories is a significant risk factor for restrictive lung function impairment. These findings underscore the importance of regular monitoring of NO levels in palm oil factories and the implementation of effective control measures to protect the respiratory health of workers.

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