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# Air Pollution-Induced Acute Respiratory Infection

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## Abstract

The respiratory system becomes the main target of the harmful effects of major air pollutants including particulate matter (PM), ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs). Particle size is directly related to potential health problems directly in the respiratory tract one of them is respiratory tract infection. The analysis shows a positive correlation between all pollutants and the incidence of acute respiratory infections. The incidence of upper respiratory tract infections, pneumonia, bronchitis and bronchiolitis that occurred in most of the pollutants studied were significantly associated with the incidence of hospitalization due to infection.

**Keywords:** air pollution, infection, respiratory tract

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## Introduction

Environmental damage due to pollution mostly causes the dominant number of illnesses in the world with an estimated 12.6 million deaths each year and is causing more than a quarter of the global disease burden. One of the causes which are a concern for WHO is air pollution, considering that nearly seven million people worldwide die each year due to diseases directly or indirectly due to air pollution. WHO data showed that 9 out of 10 people breathe air that contains high levels of pollutants. From the smog due to the disposal of motorized vehicles and smoke in the house due to cigarettes and the household kitchen. Air pollution is a major threat to people's health and climate. The combined effect of outdoor and household air pollution causes increased mortality rates from stroke, heart disease, chronic obstructive pulmonary disease (COPD), lung cancer and acute respiratory infections.<sup>1,2</sup>

WHO was collaborating with many countries to monitor air pollution and improve air quality. This program was organized because about 80% of people living in urban areas were exposed to air pollution at levels exceeding WHO guideline limits. Developing countries, especially those with low annual incomes and high population densities, suffer the highest rates of exposure to both indoor and outdoor air pollution. Irregular climate change, rapid urbanization and increasing use of non-recyclable materials were causing the highest problems for the environment. The tendency of people to burn garbage and the consumption of cigarettes, both conventional and electric, which is

increasing every year continues to produce long-term respiratory diseases that have an impact on quality of life. The same condition also occurs in developing countries including Indonesia with a high mortality rate (22%) caused by diseases due to exposure to air pollution.<sup>1,3</sup>

Air pollution raised the risk of upper and lower airway infections. Particulate matter (PM) exposure was responsible for mortality rate from respiratory infections in children and the elderly. Every annual increase of 10 g/m<sup>3</sup> in PM2.5 concentration would increase the risk of pneumonia in children by 12%. Another study also revealed an increase in NO<sub>2</sub> exposure-related pneumonia risk of up to 30%.<sup>4</sup>

## Result

### Mechanism Of Respiratory Infection Due To Air Pollution

The World Health Organization had established quality guidelines to determine the annual concentrations of PM2.5 Average of 10 g/m<sup>3</sup>. The estimated percentage of the population exposed to PM2.5 was measured using a relative risk based on an integrated exposure-response function. The concentration was determined to be respectively distributed with upper limits of 5.9 and 8.7 µg/m<sup>3</sup>.<sup>5,6</sup>

According to statistics, adult people inhaled an average of 10-15 m<sup>3</sup> of air daily and the respiratory system became the main target of the harmful effects of major air pollutants. Particle size was directly related to potential health problems because particles with a diameter of less than 10

$\mu\text{m}$  could enter directly into the blood circulation. According to Atkinson, an increase of  $10 \text{ g/m}^3$  PM2.5 particles inhaled could increase the mortality rate by around 1.04%.<sup>7</sup>

The damage caused by particulate and gaseous pollutants was determined by the concentration and solubility of inhaled pollutants versus the respiratory system's cellular defenses.<sup>8</sup> Through the endogenous production of reactive oxygen and nitrogen species (RONS), oxidative stress would initiate an inflammatory pathway.<sup>2</sup> The mitogen-activated protein kinase (MAPK) complex was involved in the activation of nuclear transcription factors such as NF- $\kappa$ B and AP-1, which stimulate the production of pro-inflammatory cytokines such as IL-8 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).<sup>11</sup>

Air pollution has also been linked to decreased regulatory T lymphocyte function, increased IgE levels, and increased production of CD4+ and CD8+ T lymphocytes, as well as a greater Th2 response to antigen stimuli, all of which are associated with chronic inflammatory diseases.<sup>10</sup>

Infections might have been caused by a variety of etiological agents, resulting in clinical conditions ranging from mild to severe. The effects were primarily mediated by an increase in pro-inflammatory cytokines, an alteration in the immune response, and an increase in viral receptor expression (ICAM-1).<sup>5</sup>

Environmental particulate matter (PM) is a suspension of particles that can enter the lower airways and cause a variety of effects.<sup>12</sup> The inflammation caused by damaged alveolar macrophages, neutrophil recruitment, disruption of barrier defenses and upregulation of receptors and molecules involved in pathogen invasion.<sup>5</sup> Because of their small particle size, PM2.5 could cause an abnormal cell cycle by overexpressing miR155 (miR155). Since miR155 induced an imbalance in inflammatory and oncogenic processes, it might contribute to susceptibility to pathogens.<sup>14</sup>

Ozone, a gas formed by the oxidation-reduction reactions of NOx precursors, would have an impact on lung and bronchial tissue. These effects are mediated by pathways involved in tissue repair and regeneration, reactive nitrogen species production, oxidative damage, and the expression of inflammatory markers such as IL-6, CXCL1, CCL2, and myeloperoxidase.<sup>15</sup>

## Air Pollution And Acute Respiratory Infection

Every  $10 \text{ mg/m}^3$  concentration of air pollution increased the risk of mortality from acute respiratory infections (ARI). A study in Indonesia discovered a correlation between all pollutants and acute respiratory infections.<sup>16</sup> Upper respiratory tract infections, pneumonia, bronchitis, and bronchiolitis were observed in most of the pollutants studied, including PM10, PM2.5, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>, and were significantly associated with the incidence of infection-related hospitalization.<sup>17</sup>

### Upper respiratory tract infection

In both children and adults, the upper respiratory tract is a common site of respiratory infections. The incidence is higher in areas with high pollution levels and high hospitalization rates. Runny nose, sneezing, and coughing with or without fever are the most common symptoms of upper respiratory tract infection. According to research, an increase in PM2.5 and PM10 concentrations above 10% was associated with a higher incidence of infection when compared to areas with low pollution.<sup>18</sup>

The mucociliary system barrier in the nose serves as the airways' first line of defense, cleaning harmful substances such as PM. The accumulation of various pro-inflammatory cytokines and chemokines caused by air pollution inhalation can affect ciliary movement and cause mucus accumulation. Children are more likely than adults to develop upper respiratory tract infections because their respiratory systems are not fully developed, the diameter of their airways is narrow, and the susceptibility to epithelial damage makes infections easier to occur.<sup>19</sup>

Furthermore, changes in the microbiota found in the pharynx could lead to respiratory tract diseases. Microbiota typically aids in the neutralization of pathogenic effects of external bacteria. Major respiratory pathogens were found in the pharyngeal microbiota after air pollution exposure. Pathogenic microbes detected in the patients' samples included *Streptococcus* sp., *Haemophilus* sp., *Moraxella* sp., and *Staphylococcus* sp.<sup>20</sup>

A meta-analysis found a significant correlation between PM10 and upper respiratory tract infection. Because PM2.5 contains small particles, it will enter the lower respiratory tract directly. In contrast to PM10, which contains larger particles and tends to settle in the upper respiratory tract. This will activate the local immune

system, causing it to recognize the antigen and begin the inflammatory process.<sup>21</sup> This process will irritate, increase epithelial permeability, and decrease mucociliary clearance, reducing the upper respiratory tract's barrier of defense against pathogenic infections. Another study discovered a significant correlation between the incidence of viral colonization that causes upper respiratory tract infections in children exposed to high levels of PM10.<sup>22)</sup>

### Pneumonia

Suspended particle concentrations and pneumonia were positively correlated due to the accumulation of inhaled polluted air for an extended period each year.<sup>23</sup> Mehta et al. reported cases stating that a 10 µg/m<sup>3</sup> increase in PM2.5 in long-term exposure was associated with a 13% increased rate of pneumonia.<sup>24</sup> One study found hospitalizations due to pneumonia strongly correlated with increasing concentration of PM2.5 for 3 consecutive days in a highly polluted area.<sup>25</sup>

Pneumonia is a lung parenchymal inflammation that affects the alveoli, terminal airway, and lung interstitial. *Streptococcus sp.* and *Mycoplasma sp.* are two common bacterial species that might have a significant role in the development of pneumonia. Normally, pulmonary host defenses routinely eliminate these microorganisms. When these host defense mechanisms are compromised, externally transposed pathogenic microorganisms can grow and displace the normal flora to overgrow and lead to infection.<sup>26</sup>

The airway epithelium serves as the first line of defense against respiratory pathogens by acting as a physical barrier between the mucociliary and immune systems. The airway epithelium initiates a variety of innate and adaptive immune responses to effectively target bacterial and viral pathogens. Typically, these defense mechanisms result in rapid pathogen clearance. Furthermore, alveolar macrophages have a strong phagocytic ability that facilitates the protection against respiratory infections.<sup>27</sup>

Environmental agents can affect the respiratory epithelium, resulting in impaired airflow filtration, mucociliary clearance, macrophage activation, and immunological defenses against pathogens. Pollutant particle exposure would result in the production of reactive oxygen species (ROS) and activate mitochondrial dysfunction, inflammatory mediator release, and apoptosis

leading to the disease.<sup>28</sup> By inducing abnormal immune function in the lungs and causing oxidative damage, air pollution may cause pneumonia. Particulate inhalation reduced the intrapulmonary killing of bacteria, showing that particulate inhalation affects the respiratory tract's bactericidal activity and/or clearance mechanisms.<sup>29</sup>

### Lower airway infection

According to a global study published in 2016, lower respiratory infections (LRI) were the sixth-leading cause of death for all ages and the leading cause of death in children under the age of five.<sup>25</sup> LRI contributed to a significant number of mortality in children under the age of five and elderly people over the age of 70.<sup>30</sup> A study also found a 7% increase in adult lower respiratory tract infection with each 10 µg/m<sup>3</sup> increase in PM2.5 exposure in the previous 7 days. The incidence was increasing 15–32% in the odds ratio after 1 month of exposure.<sup>31</sup>

Lower airway infections which include bronchitis and bronchiolitis were frequently associated with viral infection. These conditions were mostly caused by Respiratory Syncytial Virus (RSV), influenza, parainfluenza, adenovirus, and human metapneumovirus. Bronchiolitis was the most common airway infectious disease in children, with RSV being responsible for 50-90% of cases.<sup>31</sup>

Bronchiolitis is typically characterized by mild inflammation and congestion in the bronchioles, and occasionally causes breathing problems that demand hospitalization. This effect was found in very young children (76.5%), but it also existed in older kids and adults.<sup>32</sup>

The negative impact of air pollution on local airways caused inflammation and disruption of the lung's innate immune system. The cytokine-mediated inflammation signaling pathways, which were directed by specific signaling proteins, appear to be the common response to both air pollution and infectious pathogens.<sup>33</sup> The upregulation of the interferon (IFN) gene production suggests that particulate air pollution had a downstream effect on the response to infection. The increased IFN activity caused by PM2.5 exposure might have a stimulatory effect on the immune system, causing it to overreact to infections and likely to result in a severe infection course. Reduced levels of α-defensin 1 and S100A7 in bronchoalveolar lavage fluid, indicated an impaired ability to resolve infection-induced inflammation.<sup>34</sup>

## Conclusion

The prevalence of acute respiratory tract infections is rising as a result of air pollution exposure. The mechanism that occurred was caused by a decrease

in mucous ciliary clearance, damage to lung innate immunity and antigen recognition mechanisms, as well as changes in respiratory tract microbiota and normal flora.

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