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An update on association of white blood cells and air pollution

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Abstract

Owing to rapid population growth and industrialization, the situation of air pollution has become a public health threat of global concern. White blood cells, also known as leukocytes or leucocytes, are immune system cells that assist in defending the body against infectious diseases and foreign intruders. White blood cells are a component of the immunological system of the body. They support the body's defense mechanisms against illness and infection. Infection or inflammation are the usual causes of an overabundance of white blood cells. A high white blood cell count may, less frequently, be a sign of some blood malignancies or bone marrow issues. Although immune system inflammatory reactions might be linked with alterations in white blood cell counts in the body, there is the need to provide more consistent reporting on the association between air pollution and varying white blood cell counts in the body

Keywords: white blood cells, air pollution, cytokines, inflammation, pollution

Introduction

Owing to rapid population growth and industrialization, the situation of air pollution has become a public health threat of global concern. According to the world health organization (WHO), about one out of every eight deaths is associated with air pollution(World Health Organization, 2014). Also, the International Agency for Research on Cancer (IARC) has defined air pollution as a Group 1 carcinogen (Loomis *et al.*, 2013). Earlier studies have reported on the association between air pollution and morbidity and mortality in humans (Bae and Kwon, 2019; Liu *et al.*, 2019; He *et al.*, 2020; Wyatt *et al.*, 2020) and have revealed many links to various diseases including stroke, cardiovascular diseases and diabetes mellitus (Yang *et al.*, 2018; Graber *et al.*, 2019; Wong *et al.*, 2020).Apart from pathogenic mechanisms, oxidative stress, genetic and epigenetic pathways, inflammation is one of the commonly accepted postulated mechanisms (Veranth *et al.*, 2006; Uren, Yuksel and Onal, 2014; Graber *et al.*, 2019; Arias-Pérez *et al.*, 2020; Wooding *et al.*, 2020).

Air pollutants could be solid particles, liquid droplets or gases. Among the various air pollutants from different sources, particulate matter (PM) has been identified to be associated with cardio-pulmonary diseases (Xing *et al.*, 2016; Bourdrel *et al.*, 2017; Graber *et al.*, 2019). The effects of particulate matter on human health depends on the size of PM inhaled. Inhaled PM > 10μm in diameter would be trapped in the upper respiratory tract, those < 10μm in diameter would reach the lower respiratory tract whereas fine PM (<2.5μm in diameter) and ultrafine PM (<0.1μm in diameter) would end up in the alveoli and even penetrate the epithelia into the blood stream (Miller, Shaw and Langrish, 2012; Ni, Chuang and Zuo, 2015; Pope *et al.*, 2016). The inhaled pollutants instigate hyper-inflammatory responses which are associated lung epithelium injuries (Feng *et al.*, 2016; Pope *et al.*, 2016; Glencross *et al.*, 2020).

White blood cells

White blood cells, also known as leukocytes or leucocytes, are immune system cells that assist in defending the body against infectious diseases and foreign intruders(Obeagu *et al.*, 2021; Obeagu *et al.*, 2014; Ogbonna *et al.*, 2021; Okoroiwu *et al.*,2021; Obeagu *et al.*, 2016; Oke *et al.*, 2022). Hematopoietic stem cells, which are multipotent bone marrow cells, are the source of all white blood cell production and development. The blood and lymphatic systems of the body both include leukocytes. White blood cells all have nuclei, which sets them apart from platelets and anucleated red blood cells (RBCs), which are the other blood cells. Cell lineage is typically used to categorize the many types of white blood cells (myeloid cells or lymphoid cells). White blood cells are a component of the immunological system of the body. They support the body's defense mechanisms against illness and infection (Monga *et al.*, 2022). Granulocytes, which include neutrophils, eosinophils, and basophils, and agranulocytes, which include monocytes and lymphocytes (T cells and B cells), are different types of white blood cells. Neutrophils, eosinophils, mast cells, basophils, and monocytes are examples of myeloid cells (myelocytes). Dendritic cells and macrophages are two further divisions of monocytes. Phagocytic cells include neutrophils and monocytes. T cells (split into helper, memory, and cytotoxic T cells), B cells (divided into plasma cells and memory B cells), and natural killer cells are lymphoid cells (also known as lymphocytes). Granulocytes and agranulocytes were historically used to categorize white blood cells according to their morphological properties; however, this approach is now less frequently utilized. White blood cells, which are made in the bone marrow, protect the body against illness and infections (LaFleur-Brooks, 20009; Monga *et al.*, 2022). Infection or inflammation are the usual causes of an overabundance of white blood cells. A high white blood cell count may, less frequently, be a sign of some blood malignancies or bone marrow issues.

Since the presence of leukocytes in the blood is frequently a sign of disease, the white blood cell count is a crucial component of the total blood count. The typical range for the white cell count is 4 109/L to 1.1 1010/L. The standard measurement for this in the US is 4,000 to 11,000 white blood cells per microliter of blood. In a healthy adult, white blood cells make up about 1% of the total volume of blood, far fewer than red blood cells, which account for 40% to 45% of blood volume (LaFleur-Brooks, 20009).

Air Pollution

From smog hanging over cities to smoke inside the home, air pollution poses a major threat to health across the globe. Almost all of the global population (99%) are exposed to air pollution levels that put them at increased risk for diseases including heart disease, stroke, chronic obstructive pulmonary disease, cancer and pneumonia. According to the World Health Organization, there is 6.7 million deaths each year from exposure to ambient and household air pollution (WHO, 2023)

Air pollution, especially fine particulate matter [PM <2.5 µm (PM2.5)], and weather variations, such as changes in temperature and humidity, are critical factors for the increased risks of respiratory and cardiovascular diseases in varied populations (Graber *et al.,* 2019). To date, one of the most widely accepted underlying mechanisms for these health effects is activation of systemic inflammatory responses. Given that systemic inflammation activates/mobilizes inflammatory cells and may change the distribution of leukocytes, exploring the associations of air pollution and weather with leukocyte distribution is important to understand the impacts of environmental exposures on the immune system (Brook *et al.,* 2010). Air pollutants come from a variety of sources. These substances are suspended in the atmosphere, and can exist in the form of solid particles, liquid droplets, and gases. PM affects human health differently depending on its size. When humans inhale PM, the large particles (>10 µm in diameter) would be trapped in the mucus lining of the upper airway (nose, trachea). If the diameter of inhaled particles is smaller than 10 µm, then they can reach the lower respiratory tract. Fine particles (PM2.5, with a diameter smaller than 2.5 µm) and ultrafine particles (UFP, with a diameter smaller than 0.1 µm) can reach the alveoli deep inside the lungs, and even penetrate through the epithelia into the bloodstream. The inhaled pollutants cause epithelium injuries and activate the immune system to launch a cascading inflammation response (Tang *et al.,* 2020)

Air pollution and white blood cells

Although immune system inflammatory reactions might be linked with alterations in white blood cell counts in the body,there is the need to provide more consistent reporting on the association between air pollution and varying white blood cell counts in the body(Emmanuel *et al.,* 2018; Obeagu *et al.,* 2017; Obeagu *et al.,* 2017; Obeagu, 2018; Okorie *et al.,* 2020; Obeagu *et al.,* 2022). For instance, Tan *et al.,* 2000 indicated that air pollution was associated with leukocyte counts in some 30 people who had been exposed to forest fires.In another study which investigated the level of pollutant exposure in 31 heathy people at different locations, it was ascertained that particulate matter was linked to the total neutrophil and monocyte counts; and then NO_2 had an inversely proportional relationship with lymphocyte and eosinophil counts (Steenhof *et al.,* 2014).Moreover, Pope *et al.,* 2016 after investigating 24 healthy adults in three study periods found that exposure to fine particulate matter (< 2.5µm in diameter) caused elevated counts of monocytes, natural killer cells, T-helper cells and killer T-cells. Contrarily,another study after investigating exposure of 38 healthy cyclists to 20 minutes on a major road indicated that higher percentages of neutrophils in the body but invariably no change in white blood cell counts (S *et al.,* 2013). Zuurbier *et al.,* 2011 investigated 34 healthy individuals who had a two-hour exposure to particulate matter during a journey and found no association between air pollution and total white blood cell count but found a negative association between air pollution and the count of

neutrophils. Stiegel *et al.*, 2016 after investigating exposure of 15 study volunteers to diesel exhaust indicated decreased counts of monocytes and lymphocytes and increased percentages of neutrophils but apparently no unchanged counts of total white blood cells.

Inflammatory reactions may be important in the development of illnesses, and research has linked air pollution to health risks(Glencross et al., 2020). One indicator of inflammation is the WBC count, although there are conflicting views in the published literature about how exposure to air pollutants affects WBC counts(Steenhof et al., 2014).

Similarly, the production of acute-phase proteins, blood circulation of inflammatory mediators, and activation and mobilization of inflammatory cells all contribute to the onset of the systemic inflammatory response(Di et al., 2021). A crucial component of the systemic inflammatory response is the release of white blood cells (WBC) and platelets into circulation, which is brought on by the stimulation of the hematopoietic system, namely the bone marrow(Di et al., 2021). Circulating WBC levels are a good predictor of effects on cardiovascular health, as shown by several large population-based studies carried out over the past few decades, even after considering other risk factors(Barnes, 2016). Up until recently, several studies have examined the link between exposure to air pollution and circulating WBC, with various degrees of success(Barnes, 2016). Nevertheless, producing pro-inflammatory cytokines through air pollution may cause an abnormal alteration in inflammatory biomarkers such as WBC, lymphocytes, neutrophils, and eosinophils(Glencross *et al.*, 2020). These four biomarkers are several subtypes of peripheral white blood cells that can gauge early-stage inflammation in the human body(Glencross et al., 2020).

The incidence and progression of several disorders, including chronic obstructive pulmonary disease and asthma, may be significantly influenced by changes in inflammatory biomarkers brought on by air pollution(Du et al., 2022). Their molecular mechanisms, however, are intricate and little understood(Du et al., 2022). According to one theory, being exposed to air pollution causes the production of pro-inflammatory mediators, which then causes the migration, infiltration, or extravasation of pertinent inflammatory cells(Wang et al., 2021). In research on animals, it was shown that rabbit alveolar macrophages could boost white blood cells by releasing bone marrow precursors, and that white blood cells then reached circulation swiftly(Miller et al., 2016).

Gaseous pollutants can also affect inflammatory indicators by promoting the production of stress and chemoattractant hormones in vivo(Uren et al., 2014). The rise and extravasation of neutrophils in the lungs were linked to the release of stress hormones brought on by O3(Miller *et al.*, 2016). Moreover, the innate neutrophilic immune response might be triggered by O3 due to elevated levels of circulating adrenaline and corticosterone(Miller *et al.*, 2016). The generation of inflammatory cytokines in the lungs and neutrophils caused by O3 in rats can be reduced by blocking the receptors for stress hormones(Du *et al.*, 2022).

Conclusion

Owing to rapid population growth and industrialization, the situation of air pollution has become a public health threat of global concern. A high white blood cell count may, less frequently, be a sign of some blood malignancies or bone marrow issues. Although immune system inflammatory reactions might be linked with alterations in white blood cell counts in the body, there is the need to provide more consistent reporting on the association between air pollution and varying white blood cell counts in the body

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