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EDITORIAL

Environment and Neurological Diseases: Growing Evidence for Direct Relationship

Mohammad Wasay and Adeel Khoja

Exposure to air pollution has been implicated in a number of adverse health outcomes. There is increasing evidence that point towards association of airborne pollutant exposure with respiratory, cardiovascular, and neurovascular pathology.[1] However, the latter receives the least attention due to paucity on literature examining the impact of polluted environment on cerebrovascular disease. It is important to note that airborne pollutants, such as particulate matter (PM), have the ability to extend beyond the respiratory system and enter the central nervous system (CNS).[2] The World Health Organization (WHO) has estimated that environmental pollution affects health outcome of every nine out of ten people in the world.[3]

Recent studies have shown air pollution and PM to be associated with neuroinflammation and production of reactive oxygen species (ROS).[4] Although the mechanisms regarding entry of PM into CNS are not well understood, PM can be trans-located along the pathway of olfactory nerve into the olfactory bulb and can cross permeable brain barriers.[5] Inhaled pollutant particles are also implicated in neuronal damage through microglial activation and increase in production of cytokines by immune cells of the brain.[3] A study has shown exposure to diesel exhaust particles, a common component of urban air pollution, causing microglial activation, dopaminergic neurotoxicity and increase in ROS production.[6] These findings suggest strong pro-inflammatory and immune upregulating capacities of air pollution; which may contribute to the pathogenesis of neurodegenerative diseases.

Air pollution is a prevalent proinflammatory stimulus to the CNS and a risk factor for neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD).[5] An alarming finding by Braak *et al*., confirmed the presence of aggregated α-synuclein in targeted areas of PD involvement in young cohorts exposed to high air pollution.[7,8] The process of accumulation and fibrillation of soluble α-synuclein (pathologic hallmark of PD) and Aβ42 (pathologic hallmark of AD) can start in early years despite having no other risk factors for neurodegenerative diseases.[7] Moreover, carriers of particular alleles have a higher risk of developing AD, if they live in a polluted environment.[7] In a study by Chen *et al*. carried out on individuals greater than 40 years of age exposed to high concentration of PM_{10} (above 65 $\mu g/m^3$), had 35 times higher chances of developing PD as compared to those exposed to low concentrations of PM_{10} (below 54 $\mu g/m^3$).[9] Having a residence in an urban area, it can lead to 9% increase risk of developing PD as compared to those living in rural areas.[10]

The impact of living in a polluted environment on stroke is under-recognised, yet substantial.[4] According to the Global Burden of Disease Study 2013, 29.2% of the global stroke burden is attributable to air pollution.[11] Furthermore, a meta-analysis of 94 studies found stroke hospital admissions to be correlated with high concentrations of carbon monoxide, sulfur dioxide and nitrogen dioxide.[12] The European Study of Cohorts for Air Pollution Effects reported that even a small increase of about 5 $\mu m/m^3$ in $PM_{2.5}$ concentration in the air was associated with 19% increase risk of stroke.[4]

Ground level ozone (O_3), an urban air pollutant, is also associated with delirious effects on CNS and cognitive impairment.[1,5] Short- or long-term exposure to O_3 may induce an inflammatory response or generate oxidative stress leading to lipid peroxidation in the brain, dopaminergic neurotoxicity and memory deterioration.[2,5] Moreover, high concentration of O_3 in the environment was associated with a 211% increase risk of AD onset.[13] A recent study showed that people living in a polluted environment having high concentrations of O_3 had a 34% faster rate of cognitive decline annually on the Mini Mental Status Examination (MMSE) as compared to those exposed to lower concentrations of O_3.[1]

Increasingly, studies have shown that PM can enter the brain and has been associated with neurovascular pathology.[5] PM exposure was also reported to cause 138% increase in risk of AD onset,[13] increase in hospital admissions for migraines by 3.3%, and for headaches by 3.4%.[14] Two fractions of PM predominantly affecting CNS are $PM_{2.5}$ and ultrafine particulate matter (UFPM); both being inhaled on a consistent basis as constituents of air pollution.[5] Histopathological examinations of postmortem brain tissue from individuals living in highly polluted areas have observed PM to be accumulated in

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neurons in the olfactory bulb and in blood vessels present in the frontal lobe and trigeminal ganglia.[7] This provides insight into PM being able to pass through the tissue barriers in the lung and brain, subsequently accumulating in the neurons and vessels.

Major roadway proximity was associated with diminished verbal memory, psychomotor speed, language, and executive functioning.[4] A population based cohort study of 2.2 million individuals, demonstrated a significant association between major roadway residence and dementia incidence.[15] A study targeting urban population showed that residents who were exposed to high traffic-related air pollution had 40% more chances of developing dementia or AD.[16] The study also reported that increase in incidence was greater than 70% in a subpopulation excluding younger adults.[16] These studies highlight the significance of urban air pollution with cognitive decline and neurodegenerative diseases.

These findings may have important implications for Pakistan as according to a recent World Bank report, Pakistan's urban air pollution is among the most severe in the world.[17] Notable contributors to this pollution are, including but not limited to; burning of biomass solid fuels and untreated wastewater from urban and industrial sources.[18] The potential role of air pollution in the incidence of neurodegenerative disorders and its adverse impact on health cannot be neglected.

The above discussion highlights the need for additional robust observational and experimental studies highlighting harmful air pollutants and their association with common neurological disorders. Reliable data collections and formidable interventions are key components for reducing air pollution, environmental hazards and neurodegenerative diseases. Safety measures and effective strategies to curb air pollution need to be implemented alongside increase in public awareness.

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