A Systematic Review of Air Quality Levels and SLE Rates Among Developed and Developing Countries

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Abstract:

Research on the impact of air pollution on Systemic Lupus Erythematosus (SLE) patients worldwide has consistently shown a correlation between high pollution levels and increased health complications. This includes more hospitalizations and disease activity in SLE patients, particularly in areas with poor air quality management practices.

The presence of harmful substances (i.e. particulate matter, nitrates, lead, carbon monoxide, and ozone) in the air pose health risks for SLE patients. Prolonged exposure to air pollution can trigger inflammation and oxidative stress, exacerbating conditions like SLE and impacting various organs.

Developing countries tend to have higher SLE incidence rates due to elevated gas and particle levels in the air, emphasizing the need for protective measures. Exposure to pollutants, such as PM2.5, PM10, SO_2, NO_2, and ozone, is associated with increased inflammatory markers and disease activity in SLE patients.

Overall, this research highlights the importance of monitoring and improving air quality to reduce the health risks and mortality rates associated with SLE, particularly in developing countries facing economic challenges in managing pollution levels.

Introduction:

Prolonged exposure to air pollution has been correlated with an increased susceptibility to autoimmune diseases, with research indicating that concentrations exceeding specific thresholds are linked to a heightened risk of autoimmune disease development [1]. Consequently, there is a critical imperative to delve deeper into the threshold levels that may precipitate the onset of one particular disease: SLE.

Air quality is typically evaluated using the air quality index (AQI), which serves as a metric to gauge the level of pollution present or anticipated in a specific area. Air pollution, characterized by the introduction of harmful foreign substances, poses significant risks to human health. Particulate matter (PM10 or PM2.5), nitrates (NO), lead, carbon monoxide (CO), sulphur dioxide (SO_2), ozone (O_3), as well as potentially harmful byproducts from cigarette and tobacco smoke, collectively contribute to air pollution [2].

Particulate matter encompasses a mix of hazardous chemical compounds containing pollutants like sulfates, metals, ions, and harmful organic substances, with varying diameters of 2.5 micrometers or 10 micrometers, both posing health hazards. Urban areas often witness the emission of these particles from automobile tailpipes. Fine particles, with a diameter of 2.5 mm or less, and ultrafine particles, with an average diameter below 0.1 mm, are of particular concern [3]. The adsorption molecules of particulate matter can contain significant quantities of sulfates, nitrates, metals, hydrocarbons, and other compounds [4].

Extensive global research has highlighted the detrimental impact of air pollution on the mortality and morbidity rates of chronic diseases, underscoring its severe consequences on human health [5]. Air pollution is recognized as a key environmental factor contributing to inflammation and autoimmune diseases, primarily due to its pro-inflammatory effects. Inhaled pollutants have the potential to trigger inflammation and oxidative stress, linked to both short-term and long-term respiratory conditions, systemic inflammation, and immune-mediated disorders [2].

SLE is an autoimmune rheumatic condition characterized by immunological complex depositions and impaired immunological modulation [6]. Investigation indicated that environmental variables, such as air pollution, could trigger the genetic component of SLE to develop, causing devastating consequences on numerous organs, including joints, the skin, the central nervous system, and kidneys [7].

Study Rationale:

Investigate the potential correlation between elevated pollutant levels and the incidence of SLE in both developed and developing countries by analyzing SLE cases during and post periods of heightened pollution.

Methods:

This study used an integrated cohort and observational approach to examine the occurrence of SLE across diverse geographical regions and its correlation with air quality. The literature review adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) methodology [8].

Inclusion criteria for the study encompassed factors such as the incidence ratio and prevalence of SLE, with a focus on markers like hospitalization and clinic visits following increases in air pollutants. Participants of any sex, ethnicity, or national background were considered eligible for inclusion, provided that the studies offered detailed information on air pollutants and their concentrations in the atmosphere. Studies failing to meet these specified parameters were excluded.

Exclusion criteria involved filtering out papers published before 2000, publications that referenced autoimmune conditions without explicit mention of SLE, duplication of prior studies, limited accessibility, non-English articles, and studies that did not align with the predefined inclusion criteria.

Electronic searches on PubMed Online and Scopus utilized key terms and combinations such as “SLE”, “lupus”, “systemic lupus erythematosus”, “autoimmune disorders”, “air quality”, “developing nations”, “developed countries”, “SLE incidence”, “environment and SLE”, and “air and SLE”. The search spanned up to the summer of 2022, resulting in the identification of 119 papers, with duplicates removed to yield 87 articles. Inaccessibility due to paywalls or non-English publications further reduced the total to 18 articles. Subsequent refinement steps involved filtering out studies that conflated other autoimmune conditions with SLE and publications predating 2000, culminating in a final selection of 6 articles for analysis with 3 from developing countries (Brazil, Chile, and China) and 3 from developed countries (Taiwan, Canada, and USA) with the classification defined by World Bank's economic categorization of developed and developing economies. Figure 1 visually displays the process.

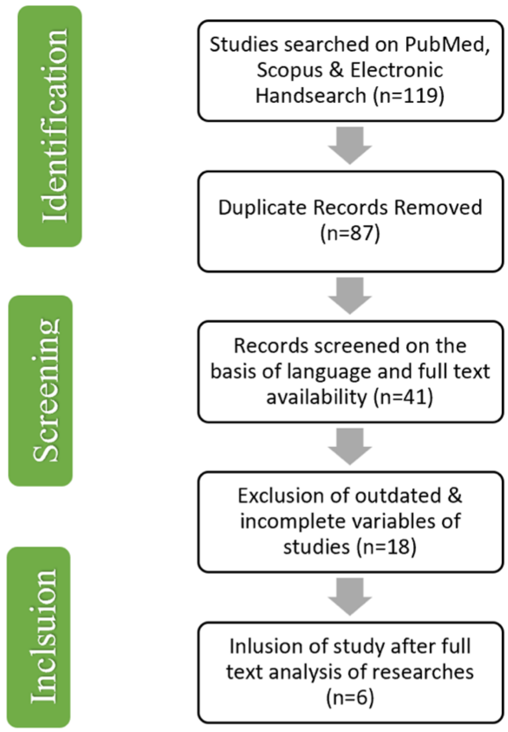

Figure 1: Study identification & selection layout.

This review encompassed data from 6,259 participants across research studies conducted in both developing and developed nations, exploring the impact of air quality on SLE rates. The study predominantly features female participants, with a distribution of 89% female and 11% male. Figure 2 visually illustrates the distribution of study participants across various research studies and their corresponding countries.

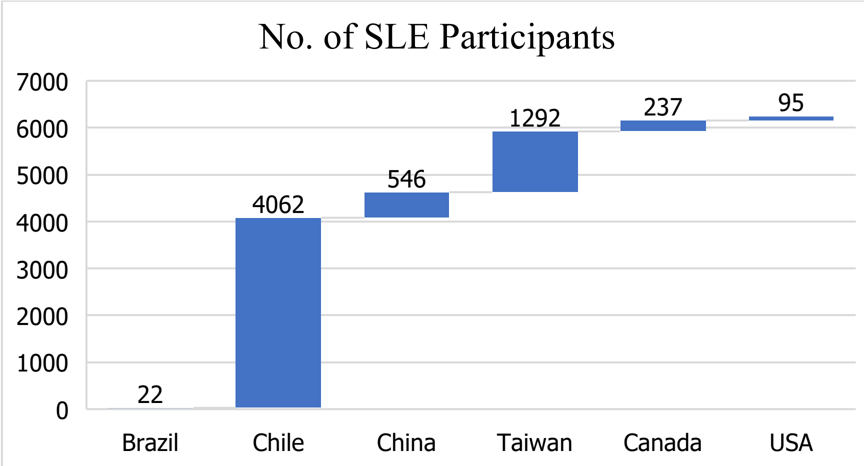

Figure 2: Number of study participants.

Analysis:

The overall analysis indicates a correlation between increased pollution levels exceeding the WHO's recommended annual average and a rise in SLE incidence. Elevated exposure to particulate matter and pollutants, like SO_2 and NO_2, heightens the risk of developing SLE. Across all countries studied, the incidence ratio averages during states of high pollution were 3.57 ± 3.28%. Notably, developing countries exhibit a significantly higher incidence rate of 5.75 ± 2.77% compared to developed countries at 1.39 ± 2.2%. This disparity is attributed to the elevated levels of gases and particles present in developing nations, emphasizing the need for protective measures for affected individuals during periods of heightened pollution. Further examination will delve into age-specific trends and the impact of various gases and particles in both developed and developing countries.

PM2.5 & PM10:

Elevated exposure levels have the potential to induce an increase in inflammatory markers [9]. The WHO guidelines stipulate an annual average concentration threshold of 5 μg/m³ for PM2.5 and 15 μg/m³ for PM10. Excessive levels of particulate matter can serve as a catalyst for heightened leukocyte infiltration, elevated levels of IgG, anti-dsDNA, and anti-nuclear antibodies, leading to significant inflammation [10]. The average PM2.5 concentration across the six studies was recorded at 33.58 ± 2.95 μg/m³, with figures of 44.96 ± 22.39 μg/m³ in developing countries and 22.2 ± 17.25 μg/m³ in developed nations. These values surpass the WHO recommendations, with levels in developing countries being double those in developed countries [11]. PM10 levels were measured at 66.26 ± 27.99 μg/m³ in developing countries, while data for developed countries on PM10 concentrations was not available.

NO_2:

Elevated levels of CRP and Interleukin-17 have been documented following exposure to NO_2, both of which are significant in the pathophysiology of SLE [12]. Furthermore, NO_2 has been associated with an escalation in the SLE Disease Activity Index (SLEDAI) score among SLE patients [12]. The WHO guidelines recommend an annual average NO_2 concentration not exceeding 10 μg/m³ [11]. Our analysis of air quality parameters extracted from the research articles revealed an average NO concentration of 59.91 ± 24.69 μg/m³. Specifically, developing countries exhibited higher average NO_2 levels at 66.22 ± 26.0 μg/m³, while Taiwan reported a lower concentration of 40.98 ± 12.42 μg/m³. The studies from the USA and Canada did not provide NO_2 data.

SO_2:

SO_2 has the potential to irritate the respiratory tract, exacerbate inflammation, and potentially lead to lung complications such as pleuritis, lupus pneumonitis, and pulmonary hypertension in SLE patients. WHO guidelines specify that the annual average concentration of SO_2 should not surpass 20 μg/m³ [11]. Both China and Chile have recorded levels exceeding this recommendation. Data on SO_2 concentrations in the USA and Canada were not available.

Ozone:

An analysis conducted by Thompson et al. demonstrated a significant and positive association between ambient air pollution, interleukins, and fibrinogen, with O_3 levels being linked to increased interleukin 6, a pro-inflammatory cytokine [13]. According to WHO guidelines, the annual average concentration of ozone should not exceed 100 μg/m³ over an 8-hour period [11]. In our study, the total data showed O_3 levels of 73.20 ± 32.67μg/m³. Developing countries exhibited a mean of 90.54 ± 31.7μg/m³, while developed countries had levels at 47.19 ± 0.72μg/m³.

CO:

CO is a potent and hazardous component of air pollutants that can trigger a rapid and excessive immune response via nitrosative stress, oxidative stress, and systemic inflammation [14]. The WHO recommends that CO should not exceed 10 μg/m³ (or 3.82 ppm) for a maximum daily of 8 hours [11]. Our study revealed the total carbon monoxide level to be under the recommended levels for all countries.

Age:

The mean age of the study cohort was calculated to be 31.96 ± 10.88 years (95% CI: 18.45-45.47). The study by Chakmak et al. highlighted a higher incidence of SLE and SLE-related hospitalizations among individuals aged over 30 years, particularly in females [15]. Similarly, the research by Jung et al. indicated a greater prevalence of SLE in older females (HR = 6.34; 95% CI: 5.42-7.42). Additionally, a significant association between SLE comorbidities and an age of 49 years or older was observed [16]. These findings suggest that advanced age may render individuals more vulnerable to environmental pollution and the onset of SLE.

Table 1: Table depicting various characteristics of the research articles reviewed.

Study	Year	Location	SLE patients	M/F	Age	IR	NO_2	SO_2	O_3	CO	PM 2.5	PM10
		Country	n		Years	%	µg/m³	µg/m³	µg/m³	ppm	µg/m³	µg/m³
Developing												
Fernandes [3]	2015	Brazil	22	2/20	15.3	5.37	80.87 ± 18.30	8.72 ± 1.95	80.85 ± 14.64	1.41 ± 0.47	-	38.02 ± 10.96
Chakmak [15]	2020	Chile	4062	475/3587	-	8.7	81.59	23.10	125.98	0.96	29.13	66.78
Zhao CN [6]	2019	China	546	45/501	38.4	3.2	36.20 ± 14.60	21.60 ± 7.69	64.80 ± 26.70	0.0009	60.80 ± 33.60	94.0 ± 47.50
Developed												
Jung [16]	2019	Taiwan	1292	182/1110	30.8	0.18	40.98 ± 12.42	15.30 ± 5.13	46.68 ± 11.0	0.59 ± 0.14	34.4 ± 7.6	-
Bernatsky [17]	2011	Canada	237	14/237	31.0	0.004	-	-	47.7 ± 23.7	-	10.0 ± 7.8	-
Finchk [18]	2006	USA	95	0/95	44.3	4.0	-	-	-	-	-	-

Results and conclusion:

There exists a consistent correlation between air pollution and heightened SLE-related health complications across diverse geographical regions. The study indicates that air pollution levels exceeding the WHO's recommended averages, stemming from sources like traffic/ factor emissions or ambient particulate matter, may be linked to increased hospitalizations and disease activity in SLE patients.

As pollution levels escalate, so do the occurrences of adverse health events. Furthermore, these pollutants likely contribute to a higher frequency of hospital admissions among SLE patients, exacerbating the negative impacts associated with the condition. Notably, developed nations demonstrate lower incidences and impacts of SLE during periods of heightened air pollution, attributed to air quality management practices through equipment and regulations, in contrast to developing countries facing economic challenges. Consequently, these concentrated pollutants have resulted in unfavorable outcomes, including elevated mortality rates among SLE patients.
With the escalation of global warming and the increasing frequency of fires and natural disasters that can cause increased air pollution, the risk of poor air quality will increase [19]. Therefore,

implementing strategies such as indoor air filtration or the utilization of respiratory devices may be imperative to mitigate the incidence and reactivation of SLE. Promising studies indicate the efficacy of HEPA filter masks, including N95 respirators, in reducing the cardiovascular effects of air pollution by limiting exposure to fine particles [20]. However, current research does not yet demonstrate a direct correlation between air pollution filters and a reduction in SLE incidence during periods of high pollution levels.

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