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Review

Climate change and pediatric rheumatic diseases: a growing concern

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ABSTRACT

Pediatric rheumatic diseases (PRDs) comprise a diverse group of inflammatory disorders affecting the musculoskeletal system and connective tissues, with multifactorial etiologies involving genetic and environmental factors. Climate change driven by rising greenhouse gas emissions and global warming, has profound implications for PRDs through increased air pollution, extreme weather events, and ultraviolet radiation exposure. Children with chronic rheumatic disorders, particularly those with systemic involvement, are especially vulnerable to these environmental stressors. This review explores the association between climate change and PRDs, with a focus on juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), immunoglobulin A vasculitis, Kawasaki disease, and familial Mediterranean fever (FMF).

Understanding the interplay between climate change and PRDs is crucial for developing adaptive strategies for disease management and public health interventions. Future research should focus on mitigating environmental risks and identifying protective measures to improve the outcomes of pediatric patients with rheumatic diseases.

Keywords: Air pollution, Climate change, Rheumatic diseases

INTRODUCTION

Pediatric rheumatic diseases (PRDs) encompass diverse inflammatory conditions that primarily affect many organs, particularly the musculoskeletal system and connective tissue (1). These diseases have a complex etiology, typically arising in genetically predisposed individuals under the influence of various environmental factors (1,2). Advances in our understanding of inflammation, immune dysregulation, and environmental triggers are transforming the approach to diagnosing and managing pediatric rheumatic diseases (3). However, studying the epidemiology and environmental risk factors of PRDs presents challenges due to their low incidence and heterogeneous nature (4). Research has explored a wide range of potential risk factors, including genetic predisposition, hormonal influences, perinatal conditions, the hygiene hypothesis, infections, vaccinations, antibiotic use, dietary factors, gut microbiota, trauma, physical activity, psychological stress, adverse childhood events, seasonal variations, air pollution, ultraviolet radiation exposure, tobacco smoke, and other environmental pollutants (3-8).

Climate change is a major environmental challenge affecting living conditions, public health, and the future of our planet. The increasing levels of greenhouse gases [CO_2, N_2O, CH_2, ozone, etc.] are driving global warming and consequently, climate change, leading to a rise in environmental pollutants, particularly air pollution (9). Extreme weather events, worsening air quality due to forest fires, the spread of vector-borne diseases, and disruptions in healthcare access are some of the direct and indirect consequences of climate change. Children with rheumatic disorders, especially those with systemic comorbidities, are particularly vulnerable to these environmental changes and their associated health risks (10).

Recently, the impact of climate change on PRDs has received increasing attention. The most common PRDs are juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis, Immunoglobulin A vasculitis, and Kawasaki disease. Familial Mediterranean fever is prevalent in the Mediterranean and Middle Eastern regions, including our country. Although these conditions share some overlapping features, they differ in etiology, clinical presentation, prognosis, and treatment strategies. In this article, we review the relationship

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Table I: Characteristics of studies on the relationship between Pediatric rheumatic diseases and climate-related parameters and air pollution

Disease	Ref.	Country	Method	CAFP	Weather/ Climate	
					Parameters	Conclusion-Suggestions
JIA	8	Israel	Case/control (558/104058)*	-	Seasonality of birth	Gender-specific birth month rhythmicity in enthesitis-related arthritis suggests in utero or perinatal autoimmune triggering by seasonal environmental factors.
JIA	18	Australia	Case/control (202/202)*	Vitamin D status	Sunlight exposure	Lower exposure to sunlight and thus UVR may increase the risk of JIA.
JIA	5	Taiwan	Case/control (2363/23630)*	Gestational age Birth weight Socioeconomic status Maternal age M/G Dis. Maternal SARDs	CO, NO_2, PM2.5, SO_2	$PM_{2.5}$ exposure from 11–40 gestational weeks to 1–14 weeks after birth can increase the risk for PRDs in a non- linear dose-response fashion.
JIA	13	Brazil	Case/control (66/125)*	GP factors Inhalable environmental elements† (pregnancy and after birth)	PM_{10}, SO_2, NO_2, O_3, CO	Cigarette smoke exposure (intrauterine and after birth) and exposure to O_3 in the second year of life were identified as potential risk factors for JIA
JIA SLE DM	16	Brazil	Time-series (2922)*	Short-term trend Seasonality Holidays Temperature Humidity	PM_{10}, SO_2, CO, NO_2 O_3	The SO_2 interquartile range (7.79 µg/ m3) was associated with an increase of 1.98% in the number of hospital admissions of PRDs due to outcome studied after 14 days of exposure.
JIA	19	Taiwan	Cross sectional Comparative (52)*	-	Temperature, Humidity Barometric pressure etc.	A dramatic weather change such as a sudden cold wave might significantly influence the experience of joint pain.
JIA	20	Canada	Multicenter Descriptive (221)*	-	Season of disease onset	No seasonal pattern was found in sJIA onset.
JIA	17	USA	Case crossover Multicenter (253)*	-	$PM_{2.5}$	Statistically insignificant PM2.5- sJIA. The $PM_{2.5}$-sJIA association is most suggestive in preschool aged children.
JIA	21	Israel	Multicenter Retrospective Descriptive (59)*	-	Seasonal peak onset of sJIA	There is no seasonal pattern.
SLE DM IgAV-HSP	5	Taiwan	Case/control (2363/23630)*	Gestational age, Birth weight Socio-economic status Maternal age, M/G Dis. Maternal SARDs	CO, NO_2, $PM_{2.5}$, SO_2	$PM_{2.5}$ exposure from 11–40 gestational weeks to 1–14 weeks after birth can increase the risk for PRDs in a non-linear dose- response fashion.
SLE	26	USA	Regression (1628)*	Age Gender Income Racial distribution Rural vs. urban residence	$PM_{2.5}$ Ozone Temperature Residual wind, Relative humidity Barometric pressure	There is a strong association between changes in atmospheric and environmental variables ten days prior to patient visit and organ specific lupus activity at the visit.
SLE	32	Canada	Clinical cohort (237)	Ozone Outdoor ambient temperatures	$PM_{2.5}$	$PM_{2.5}$ levels were associated with elevated anti-dsDNA and cellular casts, and thus SLE activity.
SLE	30	Brazil	Longitudinal Observational (9)* 108 medical appointments	Inflammatory indicators Body mass index Infections Medication	$PM_{2.5}$, NO_2 Ambient temperature Humidity	Exposure to inhalable fine particles ($PM_{2.5}$) increases airway inflammation and then pulmonary and systemic inflammation in SLE patients.

Disease	Ref.	Country	Method	CAFP	Weather/ Climate	
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SLE	33	China	Population-based Cohort (2231)*	NOx (Drinking water)	NOx (Air)	NOx in air and drinking water may be one of the important predispositions of SLE, especially for patients with renal involvement.
SLE	29	Canada	Open cohort (6 104 859)*	Age Gender Deprivation index, Urban–rural residence Smoking	$PM_{2.5}$ and ozone	$PM_{2.5}$ exposures were associated with higher risks of SARDs onset including SLE.
DM	37	Scotland Sweden Poland Netherlands Germany Japan US Canada Korea Chile Spain India Mexico Guatemala	Multticenter (919)* (468 DM, 451 polymyositis)	-	Surface UVR Sunlight Temperature Precipitation Elevation Atmospheric pressure Vapor pressure Relative humidity Wind speed Absolute latitude	Surface UVR intensity most strongly contributed to the relative proportion of DM and was strongly related to the proportion of anti-Mi-2 autoantibodies (weighted r = 0.939, p<4x10(-7) and weighted r=0.69, p= 0.020, respectively). UV radiation exposure may modulate the clinical and immunologic expression of an autoimmune disease in different populations around the world.
DM	42	China	Time-series	-	Temperature Relative humidity Wind speed $PM_{2.5}$,NO_2, SO_2, O_3, CO	Exposure to low temperature, extreme relative humidity, and temperature changes were associated with an increased risk of DM outpatient visits.
DM	40	USA Canada	Retrospective Observational (210)* (164 juvenile and 46 adult)	Photoprotective measures Smoking Infections Medications Vaccines, Stressful life events Physical activity	Sunlight exposure	Sun exposure (p=0.030; OR =2.0, 95% CI: 1.1, 3.7) associated with disease flare. Patients who flared more frequently spent time outdoors (but <30 min/day) compared with those who did not flare (p=0.040; OR = 2.5, 95% CI: 1.1, 6.1).
DM	36	Brazil	Case/control (20/50)*	Environmental inhalation exposure during pregnancy‡	PM_{10}, SO_2, NO_2, O_3, and CO	The highest tertile of tropospheric CO (3.2–5.4 parts per million) in the third trimester of gestation were significantly associated with juvenile DM. Inhaled pollutants and tobacco smoking during fetal development may contribute to juvenile DM.
IgAV-HSP	43	Korea	Ttime series (16940)*	Respiratory viruses§ Enteric viruses‖	Seasonality of disease onset	Pediatric HSP incidence shows age-related seasonal variation linked to infectious exposure.
KD	55	Canada	Multifactorial etiologic model (5616)*	Population composition Aeroallergen exposure Atmospheric concentration of spores and algae, Incidence of healthcare encounters for bacterial pneumonia or viral intestinal infections	$PM_{2.5}$, NO_2, O_3, SO_2 and CO	In this study, an association between higher atmospheric concentration of SO_2 and NO_2 and increased risk of KD was noted.
KD	57	Japan	Retrospective observational (185)*	Epidemic conditions of 14 infectious diseases	Ambient air Temperature Atmospheric pressure Relative air humidity Precipitation, Sunshine duration Wind velocity NO, NO_2, SO_2	The incidence of Kawasaki disease had positive associations with preceding hot temperature and increased concentrations of nitric oxide and sulfur dioxide and a negative association with epidemic herpangina.
KD	58	South Korea	Time-stratified Case-crossover (51486)	Temperature Relative humidity	PM_{10}, $PM_{2.5}$, NO2, SO_2, CO, O_3	The short-term elevations in $PM_{2.5}$ and SO_2 may trigger the onset of KD among children under 5 years of age.

Disease	Ref.	Country	Method	CAFP	Weather/ Climate	
					Parameters	Conclusion-Suggestions
KD	60	Japan	Nationwide population-based longitudinal (30367)	-	Particulate matter	Early life exposure to particulate air pollution, especially prenatally, is linked to higher KD hospitalization risk (OR: 1.59 for prenatal, 1.41 for postnatal exposure).
KD	56	Italy	Correlation analysis (516)*	-	Wind direction / intensity Surface temperature Precipitation Particulate matter	Certain wind conditions are more favorable for disease onset, which are possibly associated with one or more airborne agents.
FMF	66	Türkiye	Descriptive (275)*	Emotional stress Tiredness Long-duration standing /travel Starvation High intake of food, Trauma Infection	Cold exposure	One of the most common triggering factors for the attacks with serositis were cold exposure.
FMF	67	Türkiye	Descriptive study n= 882	Psychological stress Tea and coffee Mense Menopause Post-menopause Long-duration travel Relocation Starvation Sleeplessness Fatigue	Seasonal changes Cold exposure Wind exposure Humidity	Exposure to cold, humidity, seasonal changes, long-term travel, relocation and hunger may be triggers for FMF attacks, depending on the underlying mutation type.
FMF	68	Armenia	Descriptive (413)*	Emotional stress Physical exhaustion Diet (“fat” food)	Cold/ hypothermia	Regardless of the type of MEFV mutations, cold/hypothermia is one of the most common triggers for FMF symptoms in children.

:** *n,* **†:** *Occupational exposure to inhalable particles and/or volatile vapor, exposure to cigarette smoke, and the presence of industrial activities or gas stations near the home, work, daycare, or school,* **‡:** *occupational exposure to demolition, chalk, construction and/or quarry dust, paints, varnish, gasoline vapor, and/or battery fluids; stationary sources of inhaled pollution near the mother’s home; and maternal tobacco exposure,* **§:** *adenovirus, parainfluenza virus, respiratory syncytial virus, influenza virus, coronavirus, rhinovirus, bocavirus, and metapneumovirus,* **‖:** *Rotavirus, norovirus, enteric adenovirus, and astrovirus,* ***JIA: *Juvenile idiopathic arthritis,* ***CAFP:*** *Confounding/ Adjusted factors Other Parameters,* ***SLE:*** *Systemic Lupus Erythematosus,* ***DM:*** *Dermatomyositis,* ***IgAV-HSP:*** *IgA vasculitis Henoch-Schonlein Purpura,* ***KD:*** *Kawasaki disease, FMF: Familial Mediterranean Fever,* ***Ref.:*** *References,* ***GP:*** *Gestational and perinatal,* ***PRDs:*** *Pediatric rheumatic diseases,* ***sJIA:*** *Systemic JIA, M/G* ***Dis.:*** *Maternal/gestational diseases,* ***ESR:*** *Erythrocyte sedimentation rate,* ***UVR:*** *Ultraviolet radiation,* ***MEFV:*** *Mediterranean Fever*

between climate change and pediatric rheumatic diseases, with a particular focus on the most prevalent conditions (Table I).

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease among PRDs. It encompasses several subtypes and is primarily characterized by arthritis of unknown origin that begins before the age of 16 and persists for at least six weeks. JIA classification is based on factors such as the number of affected joints, extra-articular involvement (e.g., eyes, skin, internal organs), hereditary predisposition, and specific laboratory markers. The global prevalence of JIA is estimated to range between 3.8 and 400 cases per 100.000 individuals, with an incidence varying from 1.6 to 23 per 100.000 individuals (11). The development of JIA is influenced by both internal and external antigens that trigger an exaggerated inflammatory response (6,12).

The disease’s pathophysiological cascade begins with the abnormal activation of immune cells, including T cells, B cells, natural killer (NK) cells, dendritic cells (DCs), macrophages, and neutrophils. This dysregulation leads to the production of pro-inflammatory mediators, ultimately causing joint damage and systemic complications (6).

Environmental pollutants, particularly airborne contaminants [most known; PM10, PM2,5, nitrogen oxides (NOx), sulfur

dioxide (SO_2), ozone (O_3), lead, and carbon monoxide (CO)] are believed to induce oxidative stress or inflammation, which can result in systemic autoimmune disease like JIA. These effects may even be observed as early as the perinatal period (7, 13, 14). Some studies have reported that exposure to PM2.5 in early life (11–40 weeks of gestation and the first 14 weeks after birth; odds ratios range from 1.02 to 1.08) and during the preschool period (RR = 1.76, 95% CI 1.07–2.89, per 10 µg/m3 increase in 3-day lagged moving average PM2.5) is associated with an increased risk of JIA. Similarly, exposure to ozone in the second year of life (OR: 2.76, 95% CI: 1.20–6.37, p = 0.017) and SO2 (hospital admissions due to acute PRD episodes; OR: 1.98, 95% CI: 0.25–3.69) has been implicated in disease onset and exacerbation (5, 13, 15-17). In addition to air pollution, research indicates that reduced sunshine exposure may increase the risk of JIA (18), and extreme weather conditions, including sudden cold waves associated with climate change, may exacerbate joint pain. Studies have shown significant associations between cold weather events and increased pain severity ($p < 0.01$) (19). However, no convincing correlation was demonstrated between the disease process and the seasonal pattern (20, 21).

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems and results from impaired immunological tolerance. The incidence of childhood-onset SLE ranges from 0.36 to 2.5 per 100,000 individuals, with prevalence estimates varying from 1.89 to 25.7 per 100.000 across different regions (22). While genetic factors contribute to disease onset and clinical presentation, the relatively low penetrance of SLE suggests that gene-environment interactions and environmental triggers play a crucial role in its etiology (23).

In genetically predisposed individuals, environmental factors can induce epigenetic modifications through multiple mechanisms. One key mechanism is altered DNA methylation either hypermethylation or hypomethylation which affects immune regulation, particularly in CD4+ T cells. These epigenetic modifications contribute to oxidative stress and upregulate inflammatory gene expression (24). Another pathway linking environmental exposure to autoimmunity involves the aryl hydrocarbon receptor (AhR), commonly known as the 'environmental receptor'. AhR acts as a transcriptional regulator, mediating cellular responses to environmental stimuli. Its influence on immune cell function has been associated with multiple autoimmune diseases, including SLE, underscoring the role of environmental factors in disease pathogenesis (25).

Studies investigating the adverse health effects of climate change on rheumatic disorders have identified several environmental factors that may exacerbate disease activity in SLE. Rising ambient temperatures, ultraviolet radiation, ozone levels, residual wind, relative humidity, wildfire smoke, and air pollution have been associated with increased disease flares. Specific associations have been reported between these environmental exposures and SLE flares. Exposure to $PM_{2.5}$ has been linked to an increased risk of rash flares (OR 1.03) and joint flares (OR 1.03). Higher ambient temperatures have been associated with rash flares (OR 1.07), joint flares (OR 1.05), and hematologic flares (OR 1.10). Elevated ozone levels have been correlated with an increased risk of rash flares (OR 1.013). Additionally, residual wind has been linked to joint (OR 1.04), neurologic (OR 1.10), renal (OR 1.03), and pulmonary flares (OR 1.14), while higher relative humidity has shown a significant association with joint flares (OR 1.16, $p<0.050$) (10,26,27).

Climate change-related factors are expected to influence solar ultraviolet (UV) radiation levels both directly and indirectly (28). UV radiation is known to exacerbate pre-existing SLE. Experimental studies suggest that UV-B radiation, in particular, may contribute to disease onset (OR 13.71, 95% CI 3.77–49.92) by inducing reactive oxygen species, promoting DNA damage, and altering T-cell and cytokine activity (13).

Exposure to $PM_{2.5}$, a key component of air pollution, has been associated with an increased risk of developing systemic autoimmune rheumatic diseases, including SLE (adjusted HR 1.12, 95% CI 1.08–1.15) (29). Similarly, research indicates that $PM_{2.5}$ exposure may increase respiratory and subsequent systemic inflammation in children with SLE, raising the risk of a high SLE Disease Activity Index 2000 (SLEDAI-2K ≥ 8; OR 1.47, 95% CI 1.10–1.84) (30). Furthermore, PM_{10} exposure has been linked to a 34% increased risk of heightened disease activity (SLEDAI-2K score >8; 95% CI 7.0–68.0) (31). Another study found that $PM_{2.5}$ exposure was associated with elevated anti-dsDNA levels (OR 1.34, 95% CI 1.02–1.77) and increased cellular casts (OR 1.28, 95% CI 0.92–1.80), suggesting it may trigger SLE activity (32). A study investigating the relationship between NOx, an air pollution marker, and SLE found it to be a significant risk factor, influencing both disease prevalence and mortality, especially in individuals with kidney involvement (33).

Juvenile dermatomyositis

Juvenile dermatomyositis (JDM) is an uncommon inflammatory autoimmune myositis whose cause remains unknown. Distinctive skin manifestations include calcinosis, Gottron papules, and heliotrope dermatitis. Symmetrical atrophy of the proximal muscles in children impairs daily functioning. In addition to muscle weakness, systemic symptoms, including anorexia, pain, and fever may also manifest. This condition involves multisystemic vasculitis and is likely to be accompanied by cardiovascular and cerebrovascular comorbidities, as well as pulmonary problems (34). Population-based studies estimate an annual incidence of two to three cases per million children. Although rare, JDM is the most common inflammatory myopathy in children (35).

A case-control study identified air pollutants, particularly carbon monoxide exposure during the third trimester (OR 12.21, 95% CI 1.28–115.96, p=0.030) and maternal smoking during pregnancy (OR 13.26, 95% CI 1.21–144.29, p=0.030),

as potential in utero risk factors for JDM, likely mediated by epigenetic alterations and microchimerism (36). Another multicenter myositis analysis study demonstrated that the clinical and immunological manifestations of autoimmune muscle diseases, including dermatomyositis (weighted r= 0.939, p<4 x 10-7) could be modulated by ultraviolet radiation intensity in different regions. Additionally, the study identified a strong positive correlation between dermatomyositis incidence and both temperature and altitude (37). Sun exposure, and the resulting UV radiation, is a well-established environmental factor that may contribute to DM development and exacerbation. Climate change leads to stratospheric ozone depletion, which causes a rise in UV-B radiation reaching the Earth's surface. This may contribute to the development and exacerbation of DM (38,39). In a separate study, sun exposure was found to be associated with exacerbation of dermatomyositis; patients experiencing flare were found to have a greater propensity to spend time outdoors in comparison to those who did not (OR 2.0, 95% CI:1.1-3.7, p=0.030) (40). Since children spend more time outdoors than adults, those with JDM may be particularly vulnerable to the harmful effects of solar radiation (41). A study investigating the association between climate change and dermatomyositis, using meteorological parameters, found that being exposed to low temperatures and excessive relative humidity was linked to a higher likelihood of outpatient visits for dermatomyositis (42). This suggests that both extreme heat and cold may influence disease activity through different mechanisms.

Immunoglobulin A vasculitis

Immunoglobulin A (Ig A) vasculitis (previously referred to as Henoch Schonlein Purpura (HSP)) is a prevalent form of vasculitis observed in childhood, impacting individuals from diverse ethnic backgrounds globally. Its reported incidence rate ranges from 10 to 30 cases per 100.000 children, with 90 percent occurring in children under 10 years of age (43,44). In the majority of patients, the diagnosis is established upon the observation of a rash and symptoms in the gastrointestinal, musculoskeletal, and renal systems. Children present clinically with findings of palpable purpura more prominent in the lower part of the body, abdominal pain, arthralgia or arthritis, and renal involvement, including proteinuria or hematuria (45).

The etiology of IgA vasculitis seems to be influenced by a combination of environmental, genetic, and antigenic factors. Recent research has suggested that epigenetic mechanisms, such as changes in DNA and histones, may contribute to the development of IgA vasculitis and worsen inflammatory reactions (46). While epidemiological studies consider environmental factors such as seasonal and geographical diversity, the predominant focus is on infectious agents, particularly those that induce upper respiratory tract diseases, when examining the triggers of IgA vasculitis (44,47). From a climate change perspective, alterations in temperature, precipitation, relative humidity, and air pollution are expected to influence bacterial and viral activity. Furthermore, given the susceptibility of children's immune systems to the fluctuations caused by climatic changes, shifts in both the severity and frequency of respiratory tract infections could have an adverse impact on the epidemiology and prognosis of IgA vasculitis (48). An important factor impacting the prognosis is that 30-50 % of children with IgA vasculitis suffer renal involvement, which can vary in severity from mild to end-stage renal failure. IgA vasculitis-associated renal involvement is a significant contributor to chronic kidney disease (CKD) in pediatric patients (49). Exposure to elevated levels of air pollution, particularly $PM_{2.5}$ and NO_2, over a moderate to short duration is linked to a decline in eGFR and the development of CKD (50). This situation may pose a risk for childhood rheumatic patients such as IgA vasculitis with kidney involvement.

Kawasaki disease

Kawasaki disease (KD) is an acute vasculitis that predominantly impacts arteries of the small to medium size, with a predilection for in children under five (51). While the prevalence of this condition is higher in Asian countries, particularly Japan, it can manifest in children from many ethnic backgrounds, exhibiting a worldwide distribution (52). The disease is characterized primarily by mucocutaneous changes and lymphadenopathy, accompanied by a persistent fever that lasts for a minimum of five days. In the absence of proper management and treatment, KD may result in coronary artery abnormalities, which can subsequently give rise to acquired heart disease (53).

In genetically predisposed individuals, KD is thought to result from an abnormal inflammatory response to an infectious trigger or other stimuli (51,54). Changes in climate and environmental factors have been linked to an increased risk of inflammatory and atopic diseases, including Kawasaki disease, in children exposed to pollution, allergens, and dust (55). Based on extensive epidemiological analyses of Japanese data, certain studies suggest that airborne biological or chemical particles transported by tropospheric wind over extensive distances might induce KD (52). In line with this notion, an additional study investigated the correlation between the initiation of KD and environmental variables including daily precipitation, observed local surface temperature, upper air wind regimes, and local air pollution. The results suggest that particular wind conditions may foster the dissemination of airborne agents that could potentially be linked to the initiation of the disease (56). Studies investigating elevated levels of atmospheric pollutants, which are considered to cause excessive oxidative stress and inflammatory responses in the vascular system, have shown that higher levels of $PM_{2.5}$ were associated with an increased risk of KD (OR 1.02; 95% CI 1.00–1.03). Additionally, a 1-μg/m^3 increase in NO and SO2 concentrations correlated with higher KD incidence (NO: OR 3.94; 95% CI 0.04–7.98; SO2: OR 3.60; 95% CI 1.12–6.14). Elevated temperatures (RR 1.76; 95% CI 1.01–3.07) and short-term exposure to ozone (each IQR increase in O_3 concentration at lag 0 day increased the risk of KD onset by 16.2%; 95% CI 3.6%–30.3%) were also associated with a higher likelihood of KD (51,57-59). A longitudinal study

investigating air pollution exposure during the prenatal and postnatal periods reported that there was a positive correlation between particulate air pollution exposure during pregnancy (OR 2.02, 95% CI 1.13, 3.61) and the incidence of hospital admissions related to Kawasaki disease in early childhood (60).

Familial mediterranean fever

Familial Mediterranean fever (FMF) is the most prevalent autoinflammatory disease, with individuals of Mediterranean and Middle Eastern heritage being disproportionately affected. The condition is distinguished by recurrent, self-limiting episodes of fever that are accompanied by polyserositis (61). Mutations in the MEFV gene lead to excessive inflammation, a hallmark of this autosomal recessive disorder (62). The genotype-phenotype link in FMF is not linear, and patients with the same MEFV mutations may exhibit different clinical characteristics, despite belonging to the same family (63). Since disease severity is influenced more by geographic region than by MEFV mutations, this phenotypic variability suggests a role for environmental factors in modulating symptoms (64). Episodes of FMF are often preceded by emotional or physical stress (65). In a few limited studies investigating climate-related factors or living conditions that trigger FMF attacks, humidity has been identified as a trigger for FMF attacks in individuals with exon 2 mutations (p=0.023). Seasonal changes were significantly associated with increased attacks in patients with the homozygous M694V mutation (p=0.036). Similarly, exposure to cold was linked to FMF exacerbations in those with exon 10 mutations (p=0.044) and in individuals homozygous for M694V (p=0.016). In addition, long-term travel, relocation and hunger may be triggers, depending on the underlying mutation type (66,67). The significance of cold exposure, specifically hypothermia, as an environmental component has been substantiated to be on scale with physical stress as a catalyst. Conversely, reduced cold stress due to climate change and global warming has been linked to a temporary decline in the frequency and severity of FMF attacks (66,68). In another longitudinal study, it was shown that there was no significant seasonal variation in disease activity for FMF. However, it was noticed that the frequency of attacks increased during the winter season and reduced during the summer season (69).

CONCLUSION

In conclusion, when reviewing the existing body of literature, substantial evidence emerges that highlights the adverse impacts of climate change and global warming on the well-being of children. These effects manifest through alterations in seasonal patterns and atmospheric conditions, raised pollution levels, and the consequential influence on our biological, physical, and chemical surroundings. Rheumatic disorders chronically affect the life of children, rendering them more susceptible to fragility. Thus, in order to figure out the elements that delineate the onset and progression of these diseases and to develop strategies for long-term prevention and individualized therapeutic approaches, further investigation is required to analyze consequences of climate change, which stands as one of the most significant challenges of our era.

Contribution of the authors

Yaman Artunç N: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Yalçin S:*** Constructing the hypothesis or idea of research and/or article Planning methodology to reach the conclusions, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar.

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Conflict of interest

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REFERENCES

1. Bhattarai D. Inflammatory Diseases of the Eye, Bowel, and Bone in Children. Indian J Pediatr. 2024; 91: 1065-71. https://doi.org/10.1007/s12098-023-04877-2
2. Rider L, Miller F. Environmental factors in pediatric systemic autoimmune diseases. The Rheumatologist. Available from: www the-rheumatologist org/article/environmental-factors-pediatric-systemic-autoimmune-diseases. 2017.
3. Cassidy JT, Petty RE, Laxer RM, Lindsley CB. Textbook of pediatric rheumatology E-Book. 8th edn. Elsevier Health Sciences2011.
4. Correll CK. Role of Environment in Pediatric Rheumatic Diseases. Rheum Dis Clin North Am. 2022; 48: 287-304. https://doi.org/10.1016/j.rdc.2021.09.007
5. Wang CM, Jung CR, Chen WT, Hwang BF. Exposure to fine particulate matter (PM(2.5)) and pediatric rheumatic diseases. Environ Int. 2020; 138: 105602. https://doi.org/10.1016/j.envint.2020.105602
6. Zaripova LN, Midgley A, Christmas SE, Beresford MW, Baildam EM, Oldershaw RA. Juvenile idiopathic arthritis: from aetiopathogenesis to therapeutic approaches. Pediatr Rheumatol Online J. 2021; 19: 135. https://doi.org/10.1186/s12969-021-00629-8
7. Clarke SLN, Mageean KS, Maccora I,Harrison S, Simonini G, Sharp GC, et al. Moving from nature to nurture: a systematic review and meta-analysis of environmental factors associated with juvenile idiopathic arthritis. Rheumatology (Oxford). 2022; 61: 514-30. https://doi.org/10.1093/rheumatology/keab627
8. Berkun Y, Lewy H, Padeh S, Laron Z. Seasonality of birth of patients with juvenile idiopathic arthritis. Clin Exp Rheumatol. 2015; 33: 122-6.

9. Artunç NY, Yalçın SS. Çevresel kirleticiler ve küresel ısınma. In: Yalçın SS (ed.). A Multi-Disciplinary Analysis of Global Climate Change and its Effects From Childhood To Adult 1st edn. Türkiye Klinikleri Ankara, Türkiye, 2022; 6-12.
10. Bush T. Potential adverse health consequences of climate change related to rheumatic diseases. J Clim Change Health. 2021; 3: 100029. https://doi.org/10.1016/j.joclim.2021.100029
11. Al-Mayouf SM, Al Mutairi M, Bouayed K, Habjoka S, Hadef D, Lotfy HM,et al. Epidemiology and demographics of juvenile idiopathic arthritis in Africa and Middle East. Pediatr Rheumatol Online J. 2021; 19: 166. https://doi.org/10.1186/s12969-021-00650-x
12. Barut K, Adrovic A, Sahin S, Kasapcopur O. Juvenile IdiopathicArthritis. Balkan Med J. 2017; 34: 90-101. https://doi.org/10.4274/balkanmedj.2017.0111
13. Franca CMP, Sallum AME, Braga ALF, Strufaldi FL, Silva CAA, Farhat SCL. Risk Factors Associated with Juvenile Idiopathic Arthritis: Exposure to Cigarette Smoke and Air Pollution from Pregnancy to Disease Diagnosis. J Rheumatol. 2018; 45: 248-56. https://doi.org/10.3899/jrheum.161500
14. Horton DB, Shenoi S. Review of environmental factors and juvenile idiopathic arthritis. Open Access Rheumatol. 2019; 11: 253-67. https://doi.org/10.2147/OARRR.S165916
15. Zeft A, Prahalad S, Lefevre S, Clifford B, McNally B, Bohnsack JF, et al. Juvenile idiopathic arthritis and exposure to fine particulate air pollution. Clin Exp Rheumatol. 2009; 27: 877-84.
16. Vidotto JP, Pereira LA, Braga AL, Silva CA, Sallum AM, Campos LM, et al. Atmospheric pollution: influence on hospital admissions in paediatric rheumatic diseases. Lupus. 2012; 21: 526-33. https://doi.org/10.1177/0961203312437806
17. Zeft AS, Prahalad S, Schneider R, Dedeoglu F, Weiss PF, Grom AA, et al. Systemic onset juvenile idiopathic arthritis and exposure to fine particulate air pollution. Clin Exp Rheumatol. 2016;34(5):946-52.
18. Chiaroni-Clarke RC, Munro JE, Pezic A, Cobb JE, Akikusa JD, Allen RC, et al. Association of increased sun exposure over the life-course with a reduced risk of juvenile idiopathic arthritis. Photochemistry and photobiology. 2019;95(3):867-73. https://doi.org/10.1111/php.13045
19. Tsai WS, Yang YH, Wang LC, Chiang BL. Abrupt temperature change triggers arthralgia in patients with juvenile rheumatoid arthritis. J Microbiol Immunol Infect. 2006; 39: 465-70.
20. Feldman BM, Birdi N, Boone JE, Dent PB, Duffy CM, Ellsworth JE, et al. Seasonal onset of systemic-onset juvenile rheumatoid arthritis. J Pediatr. 1996;129(4):513-8. https://doi.org/10.1016/S0022-3476(96)70115-4
21. Uziel Y, Pomeranz A, Brik R, Navon P, Mukamel M, Press J, et al. Seasonal variation in systemic onset juvenile rheumatoid arthritis in Israel. J Rheumatol. 1999;26(5):1187-9.
22. Pineles D, Valente A, Warren B, Peterson MG, Lehman TJ, Moorthy LN. Worldwide incidence and prevalence of pediatric onset systemic lupus erythematosus. Lupus. 2011; 20: 1187-92. https://doi.org/10.1177/0961203311412096
23. Barbhaiya M, Costenbader KH. Environmental exposures and the development of systemic lupus erythematosus. Curr Opin Rheumatol. 2016; 28: 497-505. https://doi.org/10.1097/BOR.0000000000000318
24. Akhil A, Bansal R, Anupam K, Tandon A, Bhatnagar A. Systemic lupus erythematosus: latest insight into etiopathogenesis. Rheumatol Int. 2023; 43: 1381-93. https://doi.org/10.1007/s00296-023-05346-x
25. Wu J, Pang T, Lin Z, Zhao M, Jin H. The key player in the pathogenesis of environmental influence of systemic lupus erythematosus: Aryl hydrocarbon receptor. Front Immunol. 2022; 13: 965941. https://doi.org/10.3389/fimmu.2022.965941
26. Stojan G, Kvit A, Curriero F, Petri M. 297 Environmental and atmospheric factors in systemic lupus erythematosus: a regression analysis. Lupus Science & Medicine. 2019; 6: A215-A16. https://doi.org/10.1136/lupus-2019-lsm.297
27. Stojan G, Kvit A, Curriero FC, Petri M. A Spatiotemporal Analysis of Organ-Specific Lupus Flares in Relation to Atmospheric Variables and Fine Particulate Matter Pollution. Arthritis Rheumatol. 2020; 72: 1134-42. https://doi.org/10.1002/art.41217
28. Bais AF, McKenzie RL, Bernhard G, Aucamp PJ, Ilyas M, Madronich S, et al. Ozone depletion and climate change: impacts on UV radiation. Photochem Photobiol Sci. 2015; 14: 19-52. https://doi.org/10.1039/c4pp90032d
29. Zhao N, Smargiassi A, Jean S, Gamache P, Laouan-Sidi EA, Chen H, et al. Long-term exposure to fine particulate matter and ozone and the onset of systemic autoimmune rheumatic diseases: an open cohort study in Quebec, Canada. Arthritis Res Ther. 2022; 24: 151. https://doi.org/10.1186/s13075-022-02843-5
30. Alves AGF, de Azevedo Giacomin MF, Braga ALF, Sallum AME, Pereira LAA, Farhat LC, et al. Influence of air pollution on airway inflammation and disease activity in childhood-systemic lupus erythematosus. Clin Rheumatol. 2018; 37: 683-90. https://doi.org/10.1007/s10067-017-3893-1
31. Fernandes EC, Silva CA, Braga AL, Sallum AM, Campos LM, Farhat SC. Exposure to Air Pollutants and Disease Activity in Juvenile-Onset Systemic Lupus Erythematosus Patients. Arthritis Care Res (Hoboken). 2015; 67: 1609-14. https://doi.org/10.1002/acr.22603
32. Bernatsky S, Fournier M, Pineau CA, Clarke AE, Vinet E, Smargiassi A. Associations between ambient fine particulate levels and disease activity in patients with systemic lupus erythematosus (SLE). Environ Health Perspect. 2011; 119: 45-9. https://doi.org/10.1289/ehp.1002123
33. Chen J, Qu W, Sun L, Chen J, Kong W, Wang F, et al. The relationship of polluted air and drinking water sources with the prevalence of systemic lupus erythematosus: a provincial population-based study. Sci Rep. 2021; 11: 18591. https://doi.org/10.1038/s41598-021-98111-8
34. Gara S, Jamil RT, Muse ME, Litaiem N. Juvenile Dermatomyositis. [Updated 2023 Jan 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534236/.
35. Rosa Neto NS, Goldenstein-Schainberg C. Juvenile dermatomyositis: review and update of the pathogenesis and treatment. Rev Bras Reumatol. 2010; 50: 299-312. https://doi.org/10.1590/S0482-50042010000300010
36. Orione MA, Silva CA, Sallum AM, Campos LM, Omori CH, Braga AL,et al. Risk factors for juvenile dermatomyositis: exposure to tobacco and air pollutants during pregnancy. Arthritis Care Res (Hoboken). 2014; 66: 1571-5.https://doi.org/10.1002/acr.22358
37. Okada S, Weatherhead E, Targoff IN, Wesley R, Miller FW, International Myositis Collaborative Study G. Global surface ultraviolet radiation intensity may modulate the clinical and immunologic expression of autoimmune muscle disease. Arthritis Rheum. 2003; 48: 2285-93. https://doi.org/10.1002/art.11090
38. Barnes PW, Williamson CE, Lucas RM, Robinson SA, Madronich S, Nigel D,et al. Ozone depletion, ultraviolet radiation, climate change and prospects for a sustainable future. Nature Sustainability. 2019; 2: 569-79. https://doi.org/10.1038/s41893-019-0314-2

39. Bax CE, Maddukuri S, Ravishankar A, Pappas-Taffer L, Werth VP. Environmental triggers of dermatomyositis: a narrative review. Ann Transl Med. 2021; 9: 434. https://doi.org/10.21037/atm-20-3719
40. Mamyrova G, Rider LG, Ehrlich A, Jones O, Pachman LM, Nickeson R, et al. Environmental factors associated with disease flare in juvenile and adult dermatomyositis. Rheumatology (Oxford). 2017; 56: 1342-47. https://doi.org/10.1093/rheumatology/kex162
41. Climate Change and Children's Health. EPA. U.S Environmetal Protection Agency.
42. Chen C, He YS, Tao SS, Fang Y, Zhang RD, Fang X, et al. Climate change and daily outpatient visits for dermatomyositis in Hefei, China: a time-series study. Environ Sci Pollut Res Int. 2023; 30: 101053-63. https://doi.org/10.1007/s11356-023-29542-1
43. Hwang HH, Lim IS, Choi BS, Yi DY. Analysis of seasonal tendencies in pediatric Henoch-Schonlein purpura and comparison with outbreak of infectious diseases. Medicine (Baltimore). 2018; 97: e12217. https://doi.org/10.1097/MD.0000000000012217
44. Oni L, Sampath S. Childhood IgA Vasculitis (Henoch Schonlein Purpura)-Advances and Knowledge Gaps. Front Pediatr. 2019; 7: 257. https://doi.org/10.3389/fped.2019.00257
45. Roache-Robinson P, Killeen RB, Hotwagner DT. IgA Vasculitis (Henoch-Schönlein Purpura) [Updated 2023 Sep 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537252/.
46. Sugino H, Sawada Y, Nakamura M. IgA Vasculitis: Etiology, Treatment, Biomarkers and Epigenetic Changes. Int J Mol Sci. 2021; 22. https://doi.org/10.3390/ijms22147538
47. Wang JJ, Xu Y, Liu FF, Wu Y, Samadli S, Wu YF, et al. Association of the infectious triggers with childhood Henoch-Schonlein purpura in Anhui province, China. J Infect Public Health. 2020; 13: 110-17. https://doi.org/10.1016/j.jiph.2019.07.004
48. Mirsaeidi M, Motahari H, Taghizadeh Khamesi M, Sharifi A, Campos M, Schraufnagel DE. Climate Change and Respiratory Infections. Ann Am Thorac Soc. 2016; 13: 1223-30. https://doi.org/10.1513/AnnalsATS.201511-729PS
49. Kim WK, Kim CJ, Yang EM. Risk factors for renal involvement in Henoch-Schonlein purpura. J Pediatr (Rio J). 2021; 97: 646-50. https://doi.org/10.1016/j.jped.2021.01.008
50. Kuzma L, Malyszko J, Bachorzewska-Gajewska H, Kralisz P, Dobrzycki S. Exposure to air pollution and renal function. Sci Rep. 2021; 11: 11419. https://doi.org/10.1038/s41598-021-91000-0
51. Galeotti C, Kaveri SV, Cimaz R, Kone-Paut I, Bayry J. Predisposing factors, pathogenesis and therapeutic intervention of Kawasaki disease. Drug Discov Today. 2016; 21: 1850-57. https://doi.org/10.1016/j.drudis.2016.08.004
52. Rodo X, Ballester J, Curcoll R, Boyard-Micheau J, Borras S, Morgui JA. Revisiting the role of environmental and climate factors on the epidemiology of Kawasaki disease. Ann N Y Acad Sci. 2016; 1382: 84-98. https://doi.org/10.1111/nyas.13201
53. Kuo HC. Diagnosis, Progress, and Treatment Update of Kawasaki Disease. Int J Mol Sci. 2023; 24. https://doi.org/10.20944/preprints202308.0766.v1
54. Katz G, Wallace ZS. Environmental Triggers for Vasculitis. Rheum Dis Clin North Am. 2022; 48: 875-90. https://doi.org/10.1016/j.rdc.2022.06.008
55. Low T, McCrindle BW, Mueller B, Fan CS, Somerset E, O'Shea S, et al. Associations between the spatiotemporal distribution of Kawasaki disease and environmental factors: evidence supporting a multifactorial etiologic model. Sci Rep. 2021; 11: 14617. https://doi.org/10.1038/s41598-021-93089-9
56. Corinaldesi E, Pavan V, Andreozzi L, Fabi M, Selvini A, Frabboni I, et al. Environmental Factors and Kawasaki Disease Onset in Emilia-Romagna, Italy. Int J Environ Res Public Health. 2020; 17. https://doi.org/10.3390/ijerph17051529
57. Fujii F, Egami N, Inoue M, Koga H. Weather condition, air pollutants, and epidemics as factors that potentially influence the development of Kawasaki disease. Sci Total Environ. 2020; 741: 140469. https://doi.org/10.1016/j.scitotenv.2020.140469
58. Kwon D, Choe YJ, Kim SY, Chun BC, Choe SA. Ambient Air Pollution and Kawasaki Disease in Korean Children: A Study of the National Health Insurance Claim Data. J Am Heart Assoc. 2022; 11: e024092. https://doi.org/10.1161/JAHA.121.024092
59. Zhu Y, Chen R, Liu C, et al. Short-term exposure to ozone may trigger the onset of Kawasaki disease: An individual-level, case-crossover study in East China. Chemosphere. 2024; 349: 140828. https://doi.org/10.1016/j.chemosphere.2023.140828
60. Yorifuji T, Tsukahara H, Kashima S, Doi H. Intrauterine and Early Postnatal Exposure to Particulate Air Pollution and Kawasaki Disease: A Nationwide Longitudinal Survey in Japan. J Pediatr. 2018; 193: 147-54 e2. https://doi.org/10.1016/j.jpeds.2017.10.012
61. Sonmez HE, Batu ED, Ozen S. Familial Mediterranean fever: current perspectives. J Inflamm Res. 2016; 9: 13-20. https://doi.org/10.2147/JIR.S91352
62. Bhatt H, Cascella M. Familial Mediterranean Fever. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
63. Ben-Zvi I, Brandt B, Berkun Y, Lidar M, Livneh A. The relative contribution of environmental and genetic factors to phenotypic variation in familial Mediterranean fever (FMF). Gene. 2012; 491: 260-3. https://doi.org/10.1016/j.gene.2011.10.005
64. Ozen S, Aktay N, Lainka E, Duzova A, Bakkaloglu A, Kallinich T. Disease severity in children and adolescents with familial Mediterranean fever: a comparative study to explore environmental effects on a monogenic disease. Ann Rheum Dis. 2009; 68: 246-8. https://doi.org/10.1136/ard.2008.092031
65. Korkmaz C, Cansu DU, Cansu GB. Familial Mediterranean fever: the molecular pathways from stress exposure to attacks. Rheumatology (Oxford). 2020; 59: 3611-21. https://doi.org/10.1093/rheumatology/keaa450
66. Karadag O, Tufan A, Yazisiz V, et al. The factors considered as trigger for the attacks in patients with familial Mediterranean fever. Rheumatol Int. 2013; 33: 893-7. https://doi.org/10.1007/s00296-012-2453-x
67. Parlar K, Ates MB, Onal ME, Bostanci E, Azman FN, Ugurlu S. Factors triggering familial mediterranean fever attacks, do they really exist? Intern Emerg Med. 2024; 19: 1007-13. https://doi.org/10.1007/s11739-024-03576-w
68. Avagyan T, Budumyan A, Hayrapetyan A, Tadevosyan A. Influence of some environmental factors on manifestation of familial Mediterranean fever in children: clinical and genetic aspects. Caucaus J Health Sci Public health. 2018; 2: 1-5.
69. Acer Kasman S, Duruoz MT. Seasonal residual activity in adult familial Mediterranean fever: a longitudinal observational study. Rheumatol Int. 2022; 42: 1573-78. https://doi.org/10.1007/s00296-022-05156-7