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Trend analysis and cross-national inequity analysis of immune-mediated inflammatory diseases in children and adolescents aged 10–24 from 1990 to 2021

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ABSTRACT

Introduction: Immune-mediated inflammatory diseases (IMIDs) are chronic inflammatory diseases caused by immune system dysregulation, affecting multiple systems and organs. Children and adolescents aged 10–24 are among the high-risk groups, and the global burden is substantial.

Methods: Using the latest data from global burden of disease (GBD) 2021, we employed Joinpoint regression analysis, Socio-Demographic Index (SDI) correlation analysis, and cross-national equity analysis to elucidate the spatiotemporal differences in the burden of IMIDs among 10-24-year-olds from 1990 to 2021.

Results: The burden of IMIDs in adolescents aged 10–24, ranked by severity, includes asthma, atopic dermatitis (AD), psoriasis, diabetes, rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and multiple sclerosis (MS). Among these, asthma, AD, psoriasis, RA, and MS are more prevalent in females. Compared to 1990, the incidence rates of asthma and AD decreased in 2021, while the rates of psoriasis, diabetes, and RA increased. IMIDs are more common in Western Europe and North America, with rising incidence rates in South America and Asia. Concentration indices and slope indices indicate that these diseases are primarily concentrated in high SDI regions, although the differences in incidence rates between countries are decreasing.

Conclusion: While focusing on high-incidence regions, we must also pay attention to the incidence of IMIDs in emerging regions such as Asia and South America. Only in this way can we effectively reduce the heavy burden that IMIDs place on younger people globally.

Keywords: Immune-mediated inflammatory diseases, Children and adolescents, Global burden of disease, Joinpoint regression analysis, Average annual percentage change, Sociodemographic index, Cross-country inequality analysis

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Key messages

IMIDs are chronic inflammatory diseases caused by immune system dysregulation, affecting multiple systems and organs.
The study comprehensively elucidates the global incidence differences of IMIDs among the 10–24 age group from a temporal and spatial perspective.
Through these analyses, it reveals the patterns of IMID incidence among young populations, providing robust data support for the development of targeted health governance policies.

INTRODUCTION

Immune-mediated inflammatory diseases (IMIDs) form a category of chronic inflammatory diseases caused by immune system imbalances, encompassing a wide range of conditions including autoimmune diseases and rheumatic diseases that affect multiple organs and systems.[1] Examples include asthma, atopic dermatitis (AD), psoriasis, type 1 diabetes, multiple sclerosis (MS), inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and systemic lupus erythematosus.[1–3] Previous research indicates that although the 10–24 age group does not exhibit the highest incidence rates for these diseases, their incidence rates are still relatively high, and multiple diseases are prone to occur in this age group.[4] Asthma is the most common chronic allergic disease among children and adolescents, with most patients developing it at a young age. AD is a globally prevalent and burdensome chronic inflammatory skin disease, affecting 20% of adolescents and significantly impacting their quality of life.[5–7] Psoriasis affects 0.5% of children and adolescents worldwide.[8,9] Type 1 diabetes is the most common type of diabetes among children and adolescents, with approximately 100,000 new cases annually.[10,11] IBD, including Crohn's disease and ulcerative colitis, is a common gastrointestinal disorder, with 25% of cases diagnosed before the age of 25, severely impacting the physical and mental health of adolescents.[12,13] RA is a progressive autoimmune disease and is one of the most common chronic diseases among children, with an incidence rate of 1.6–23 new cases per 100,000 adolescents annually.[14,15] Multiple sclerosis is mostly concentrated in individuals aged 20–40, with a small portion of cases occurring before the age of 18.[16,17] While numerous studies have investigated the epidemiological characteristics of IMIDs, they primarily focus on middle-aged individuals or the general population.[4,18,19] Adolescents, as a diverse group undergoing significant physical, emotional, and psychosocial changes, have an immature immune system that is highly susceptible to these diseases.[14] The vast majority of IMIDs have unclear causes and no complete cure,[1,20] making them a significant burden for adolescents aged 10–24 and a considerable economic burden for society. Additionally, the impact of the COVID-19 pandemic on this group is substantial. Given that adolescents are a high-risk group for these diseases, our study aims to explore the spatiotemporal differences in IMID incidence among 10-24 year-olds using GBD 2021 data, in order to provide data support for alleviating their disease burden.

METHOD

Data source

The GBD 2021 provides the latest epidemiological data estimates on the burden of 371 diseases and injuries across 21 GBD regions and 204 countries and territories from 1990 to 2021.[21] All these data are available through the Global Health Data Exchange (https://www.healthdata.org/). Demographic data sourced from the United Nations (https://population.un.org/wpp/). In this study, we extracted the incidence and Years Lived with Disability (YLDs) estimates along with their 95% uncertainty intervals (UI) for psoriasis, RA, IBD, MS, asthma, type 1 diabetes (abbreviated as diabetes), and AD from GBD 2021. Additionally, we considered results in the context of the Socio-demographic Index (SDI), a composite indicator of income per capita, years of schooling, and fertility rate in females younger than 25 years. The specific calculation formula can refer to the literature.[22,23] The SDI scale ranges from near zero (indicating low development) to its maximum value (indicating high development), dividing countries and regions into 5 quintiles.[24] The SDI integrates economic, educational, and fertility metrics to provide a standardized assessment of global development

levels, facilitating cross-regional comparisons and policy formulation.[22,23] However, it overlooks internal inequalities, lacks direct health-related metrics, and is limited in sensitivity to data quality and dynamic changes. Despite these limitations, the SDI remains an effective tool for evaluating the relationship between socioeconomic development and health at a macro level, though complementary indicators are necessary to address its shortcomings.[25]

Trend analysis

We used linear regression to calculate the rates for each age group and their average annual percentage change (AAPC) by using the weighted average of the annual percentage change (APC), with the logarithmic scale rates as the dependent variable and each year as the independent variable. AAPC is calculated by fitting a log-linear regression model, where the natural logarithm of the variable ln(y) is regressed on time (t). The slope (β1) from this model represents the annual log change, which is converted to a percentage using AAPC = ($e^{\beta 1}$-1) * 100%. APC is calculated by finding the percentage change between 2 consecutive years.[26] It is computed by subtracting the previous year's value from the current year's value, dividing by the previous year's value, and multiplying by 100. We used Joinpoint regression analysis to identify trends by fitting the simplest model with multiple line segments on a logarithmic scale. Joinpoints were tested using a Monte Carlo permutation method, and the final model was selected based on the Weighted Bayesian Information Criterion. The model assumed constant variance, did not include time or country-level fixed effects, and standard errors were not clustered at the country level.

Cross-nation inequality analysis

Concentration index and slope index were used to quantify the concentrated distribution of the IMID burden across countries.[19] The slope index of inequality was calculated by regressing national YLDs rates for all age groups on an SDI-associated relative position scale, using a weighted regression model to account for heteroskedasticity. The concentration index was calculated by numerically integrating the area under the Lorenz concentration curve, which was fitted using

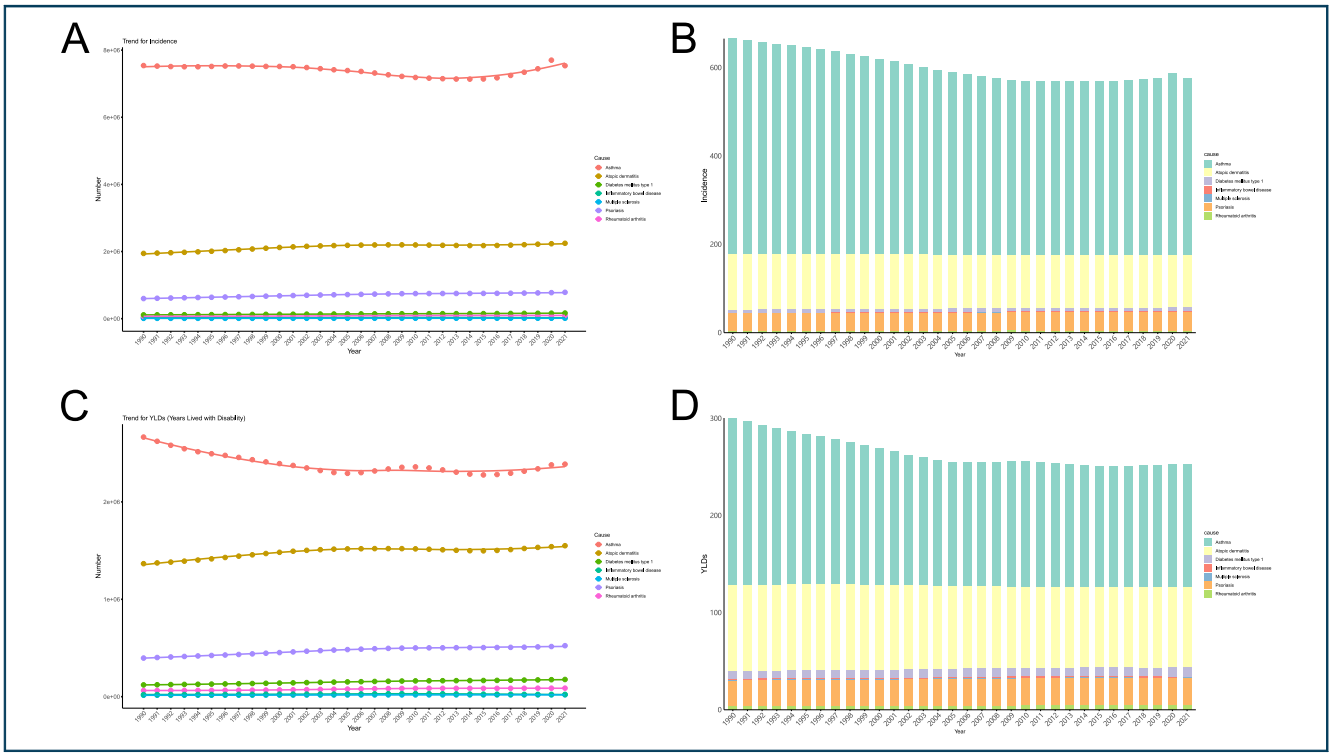


Fig. 1 Line chart of incidence (A) and YLDs (C) number and stacked cube of incidence (B) and YLDs (D) rate of 7 IMIDs from 1990 to 2021. IMID: Immune-Mediated Inflammatory Disease. YLDs: Years Lived with Disability

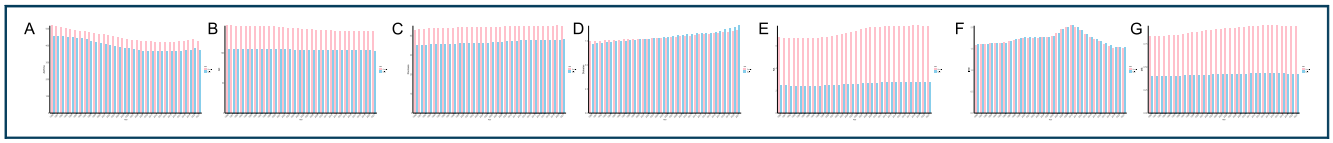


Fig. 2 Histogram of incidence rate of 7 IMIDs from 1990 to 2021 based on sex of asthma (A), AD (B), Psoriasis (C), diabetes (D), RA (E), IBD (F) and MS (G). IMID: Immune-Mediated Inflammatory Disease, AD: Atopic Dermatitis, RA: Rheumatoid Arthritis, MS: Multiple Sclerosis, IBD: Inflammatory Bowel Disease

the cumulative distribution of the population ranked by SDI and the cumulative distribution of YLDs.

Statistics

Rates were expressed as estimates per 100,000 population with their 95% UI. All analyses and visualizations were conducted using Joinpoint software and R software (V.4.3.1).

RESULTS

Global burden of 7 major IMIDs in children and adolescents aged 10-24

Globally, the incidence rate of the 7 IMIDs are ranked in the following order: asthma, AD, psoriasis, diabetes, RA, IBD, and MS. This ranking is consistent with the order of YLDs. This pattern remains consistent from 1990 to 2021 (Fig. 1, Supplementary Table 1).

In 2021, the incidence of asthma reached 7,536,121 cases (95% UI: 5,032,157 to 10,623,374) with an incidence rate of 399.21 (95% UI: 266.57 to 562.75 per 100,000). The incidence of AD was 2,245,301 cases (95% UI: 1,912,589 to 2,575,628) with an incidence rate of 118.94 (95% UI: 101.31 to 136.44 per 100,000). Psoriasis had an incidence of 784,782 cases (95% UI: 729,775 to 843,029) with a rate of 41.57 (95% UI: 38.66 to 44.66 per 100,000). MS had the lowest incidence number and rate, with 12,761 cases (95% UI: 9260 to 16,895) and an incidence rate of 0.68 (95% UI: 0.49 to 0.89 per 100,000). Regarding disease burden, the YLDs for asthma were 2,387,424 (95% UI: 1,405,402 to 3,712,213) and the rate was 126.47 (95% UI: 74.45 to 196.65 per 100,000). For AD, the YLDs were 1,550,107 (95% UI: 793,536 to 2,607,699) with a rate of 82.11 (95% UI: 42.04 to 138.14 per 100,000). Psoriasis had YLDs of 523,734 (95% UI: 378,669 to 711,892) and a rate of 27.74 (95% UI: 20.06 to 37.71 per 100,000).

In terms of gender differences, over the past 32 years, females were significantly more prone than males to develop asthma, AD, psoriasis, RA, and MS (Supplementary Table 2, Fig. 2). In 2021, the incidence rate of asthma in females was 427.08 (95% UI: 284.23 to 602.57 per 100,000), compared to 372.69 in males (95% UI: 252.53 to 530.86 per 100,000). For AD, the rate in females was 135.25 (95% UI: 115.28 to 154.74 per 100,000) versus 103.42 in males (95% UI: 87.94 to 119.09 per 100,000). Psoriasis rates were 45.07 (95% UI: 41.93 to 48.43 per 100,000) in females and 38.25 (95% UI: 35.56 to 41.16 per 100,000) in males. The rate for RA in females was 7.74 (95% UI: 5.36 to 10.51 per 100,000) compared to 2.75 in males (95% UI: 1.82 to 3.92 per 100,000). For MS, the rate in females was 0.94 (95% UI: 0.69 to 1.23 per 100,000) versus 0.42 in males (95% UI: 0.30 to 0.57 per 100,000). Interestingly, from 1990 to 1999, females had a higher incidence of diabetes compared to males. However, from 2004 to 2021, this trend reversed, with males showing a slightly higher incidence rate, although the difference was not substantial.

Joinpoint regression analysis of trends from 1990 to 2021

To explore the changes and trends in the incidence and YLDs of the 7 major IMIDs among the 10–24 age group, we conducted a joinpoint analysis (Supplementary Table 1, Fig. 3). Regarding incidence, compared to 1990, the incidence of asthma and AD significantly decreased by 2021, whereas the incidence of psoriasis, diabetes and RA significantly increased. The incidence of asthma showed a marked decline from 1990 to 2009 (1990–1996 APC: −0.82, $p = 0.000$; 1996–2009 APC: −1.26, $p = 0.000$), but the rate of decline

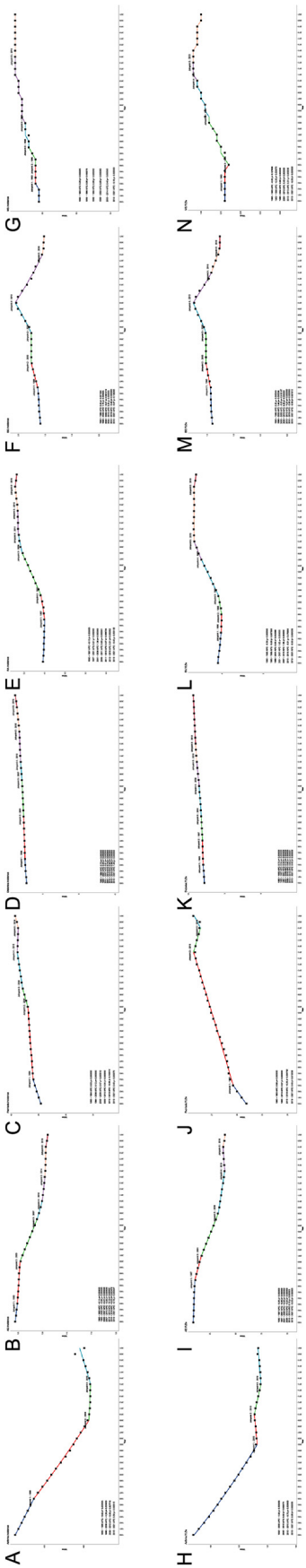


Fig. 3 Joinpoint regression analysis of incidence and YLDs rate 1990 to 2021 of asthma (A, H), AD (B, I), Psoriasis (C, J), diabetes (D, K), RA (E, L), IBD (F, M) and MS (G, N). The joinpoints have been labeled in the figure, and the corresponding APC and p (less than 0.05 is considered statistically significant) are shown in the legend. Different colors represent different segments. YLDs: Years Lived with Disability, AD: Atopic Dermatitis, RA: Rheumatoid Arthritis, MS: Multiple Sclerosis, IBD: Inflammatory Bowel Disease, APC: Annual Percentage Change

significantly slowed after 2009, and even showed an upward trend from 2015 (2015–2021 APC: 0.58, $p = 0.000$). The incidence of AD decreased most rapidly between 2000 and 2007 (2000–2007 APC: −0.41, $p = 0.000$), then the rate of decline slowed, and accelerated again during the onset of

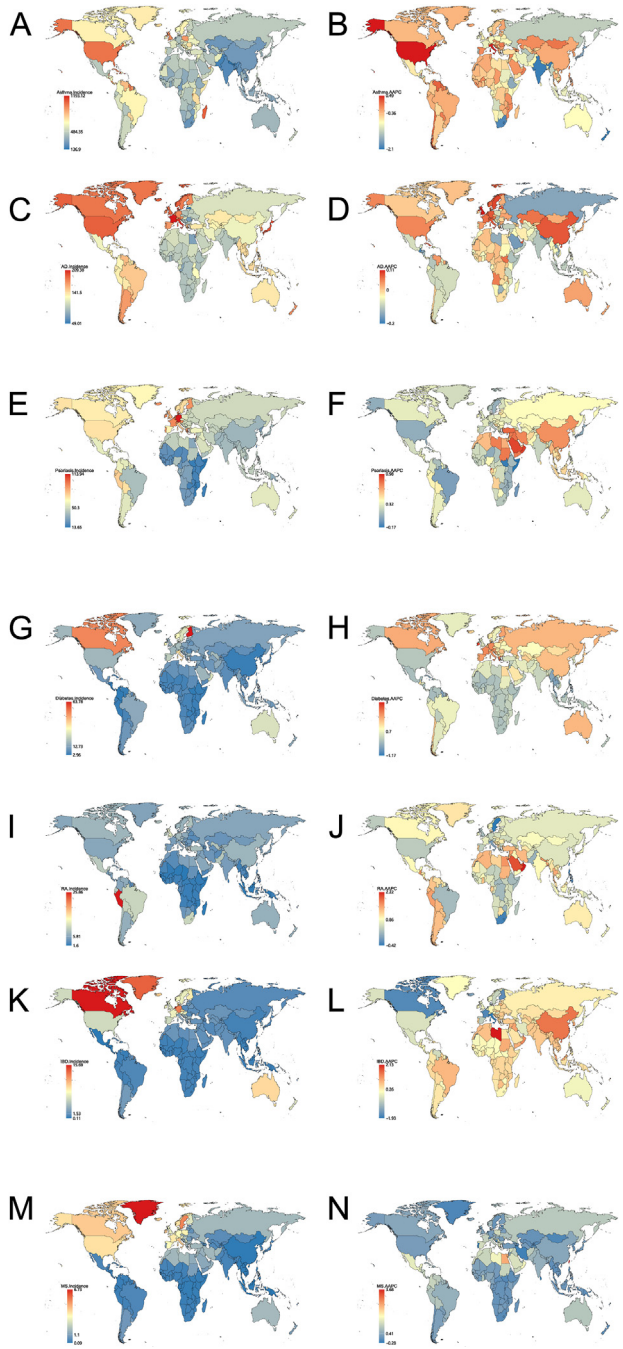


Fig. 4 Global map of 2021 IMID incidence rate and AAPC from 1990 to 2021 of asthma (A, B), AD (C, D), Psoriasis (E, F), diabetes (G, H), RA (I, J), IBD (K, L) and MS (M, N). YLDs: Years Lived with Disability, AD: Atopic Dermatitis, RA: Rheumatoid Arthritis, MS: Multiple Sclerosis, IBD: Inflammatory Bowel Disease, AAPC: Average Annual Percentage Change

the COVID-19 pandemic in 2019 (2019–2021 APC: −0.16, $p = 0.000$). The incidence of psoriasis steadily increased but showed no significant change between 2015 and 2019 ($p = 0.102$), and then increased at a faster rate after 2019 (2019–2021 APC: 0.40, $p = 0.000$). RA incidence increased most rapidly between 2001 and 2008 (2001–2008 APC: 1.36, $p = 0.000$), but showed a declining trend after 2019 (2019–2021 APC: −0.40, $p = 0.000$). The incidence of diabetes increased most rapidly from 2019 to 2021 (2019–2021 APC: 0.40, $p = 0.000$). Interestingly, the incidence of IBD peaked in 2010 and then showed a significant turnaround (2005–2010 APC: 3.22, $p = 0.000$), with a marked declining trend from 2010 to 2018 (2010–2018 APC: −3.48, $p = 0.000$). The trends in YLDs closely followed those of incidence. Notably, although the incidence of asthma continued to decline rapidly from 1990 to 2009, its YLDs stabilized around 2005.

Regional variations in IMID incidence trends

The AAPC in incidence highlights the regions experiencing the most significant increases in disease occurrence (Supplementary Table 3). The incidence of asthma in the vast majority of regions worldwide is showing a downward trend. East Asia demonstrates the highest growth in AD incidence, with an AAPC of 0.0798 (95% CI: 0.0457 to 0.114, p = 0.000), indicating a significant regional increase. Diabetes incidence is rising sharply in North Africa and the Middle East, where the AAPC reaches 3.9902 (95% CI: 3.9279 to 4.0526, p = 0.000), marking this region as a hotspot for new cases. The incidence of IBD is increasing substantially in East Asia, with an AAPC of 1.4392 (95% CI: 0.9893 to 1.891, p = 0.000), signifying rapid growth. Central Latin America exhibits the fastest increase in MS incidence, with an AAPC of 1.2717 (95% CI: 1.2436 to 1.2999, p = 0.000). In Andean Latin America, RA shows significant rise in incidence, with an AAPC of 1.3707 (95% CI: 1.3354 to 1.4061, p = 0.000). Notably, East Asia has experienced a significantly higher growth rate in the incidence of conditions such as diabetes, IBD, psoriasis, RA, MS, and AD compared to global trends. These patterns underscore the varying regional dynamics in disease incidence and emphasize the importance of tailored public health strategies to address these emerging trends.

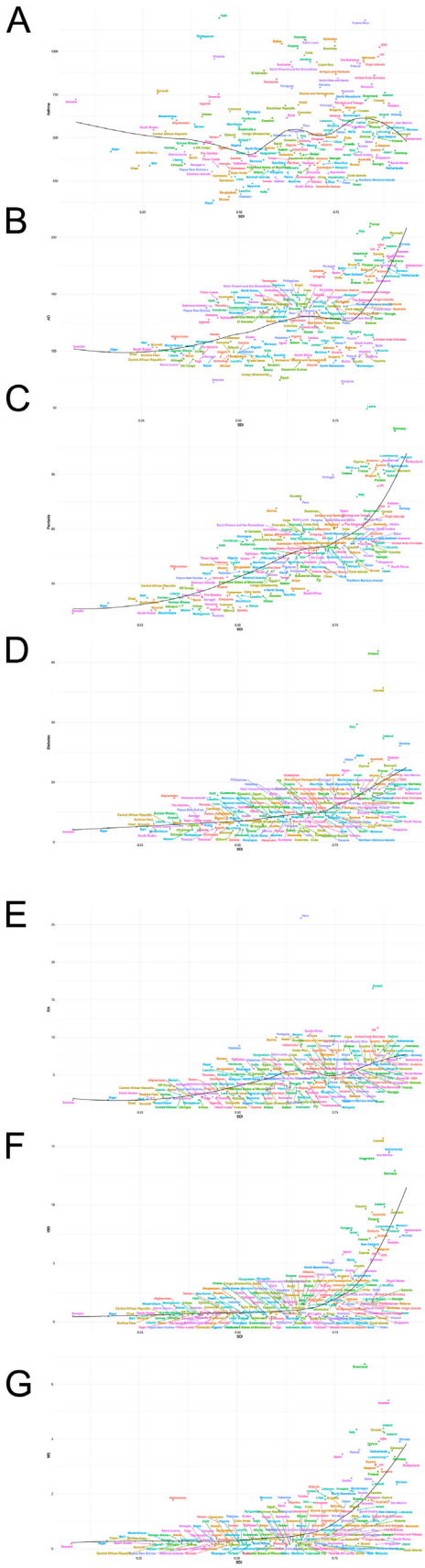
National variations in IMID incidence trends

In 2021, the incidence rates of different diseases varied significantly across countries (Supplementary Tables 4 and 5, Fig. 4). The countries with the highest asthma incidence rates were Haiti (1193.12, 95% UI: 813.90 to 1632.27), Puerto Rico (1179.42, 95% UI: 762.40 to 1700.48), and Madagascar (1075.17, 95% UI: 687.02 to 1498.92). The countries with the lowest asthma incidence rates were Pakistan (173.68, 95% UI: 119.73 to 242.18), Bhutan (157.55, 95% UI: 107.44 to 225.09), and Nepal (136.90, 95% UI: 95.85 to 191.12). The United States of America had the fastest-growing asthma incidence rate [AAPC: 0.4884 (95% CI: 0.0621 to 0.9164, $p = 0.024$)], while New Zealand had the fastest declining rate [AAPC: −2.1034 (95% CI: −2.2387 to −1.968, $p = 0.000$)].

Similarly, the highest AD incidence rates were observed in France (209.38, 95% CI: 162.42 to 261.53), Italy (203.31, 95% CI: 172.37 to 235.38), and Denmark (201.57, 95% CI: 157.44 to 247.65). The lowest AD incidence rates were in Rwanda (72.35, 95% CI: 60.18 to 84.81), Romania (71.13, 95% CI: 58.90 to 84.25), and Latvia (49.01, 95% CI: 42.37 to 56.12). The United Kingdom had the fastest-growing AD incidence rate [AAPC: 0.1132 (95% CI: 0.0879 to 0.1385, $p = 0.000$)], while the Maldives had the fastest declining rate [AAPC: −0.2016 (95% CI: −0.2264 to −0.1769, $p = 0.000$)].

The highest psoriasis incidence rates were found in Germany (113.94, 95% CI: 105.15 to 122.98), Switzerland (98.09, 95% CI: 90.17 to 106.34), and Monaco (97.46, 95% CI: 89.87 to 105.17). The lowest rates were in South Sudan (15.24, 95% CI: 14.00 to 16.45), Rwanda (13.76, 95% CI: 12.53 to 15.11), and Somalia (13.65, 95% CI: 12.58 to 14.71). The fastest-growing psoriasis incidence rate was in Equatorial Guinea (AAPC: 0.9762 [95% CI: 0.9581 to 0.9944, $p = 0.000$]), while the fastest declining rate was in Somalia (AAPC: −0.1748 [95% CI: −0.1966 to −0.1529, $p = 0.000$]).

Similarly, the highest diabetes incidence rates in the 10–24 years age group for the year 2021 were observed in Finland (63.78, 95% CI: 59.29 to



68.48), Canada (51.48, 95% CI: 46.39 to 56.44), and Italy (39.33, 95% CI: 25.46 to 56.08). The fastest-growing incidence rate of type 1 diabetes was in Cyprus [AAPC: 3.0036 (95% CI: 2.929 to 3.0783, $p = 0.000$)], while the fastest declining rate was in Saint Kitts and Nevis [AAPC: −1.1745 (95% CI: −1.3059 to −1.0429, $p = 0.000$)].

The highest incidence rates of RA among the 10–24 years age group in 2021 were observed in Peru (25.86, 95% CI: 19.04 to 34.49), followed by Kuwait (16.52, 95% CI: 11.28 to 21.94) and the United Kingdom (11.27, 95% CI: 7.95 to 15.25). The fastest-growing incidence rate of RA was in Oman (AAPC: 2.2215 [95% CI: 2.1619 to 2.2811, $p = 0.000$]), while the fastest declining rate was in Sweden (AAPC: −0.4186 [95% CI: −0.4869 to −0.3503, $p = 0.000$]).

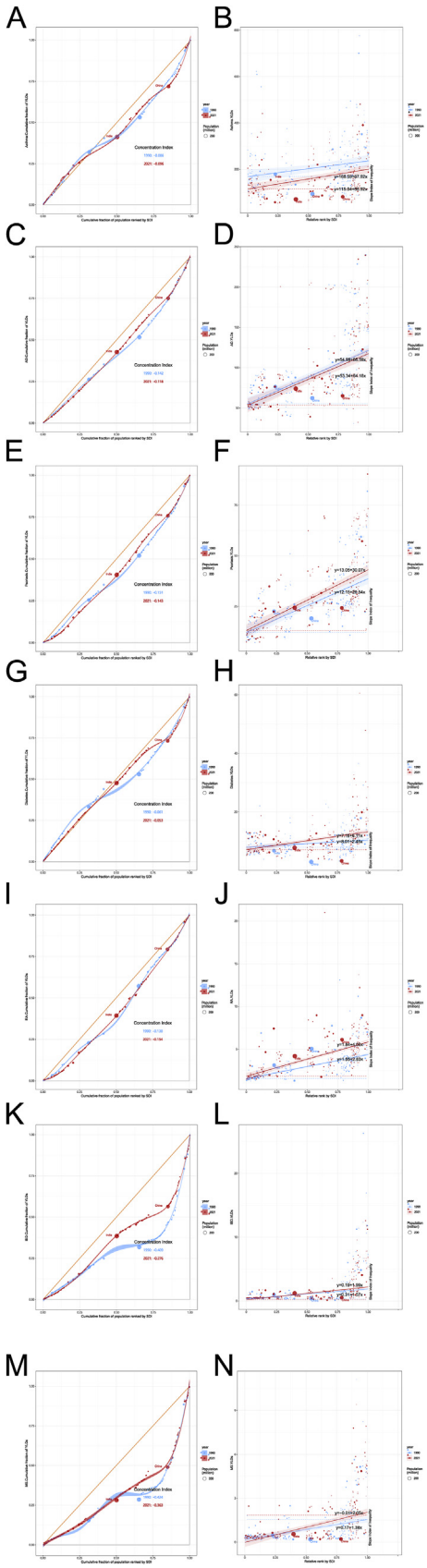
The highest incidence rates of IBD among the 10–24 years age group in 2021 were observed in Albania (3.82, 95% CI: 3.00 to 4.96), followed by Algeria (1.81, 95% CI: 1.40 to 2.35) and Afghanistan (1.37, 95% CI: 1.04 to 1.75). The fastest-growing incidence rate of IBD was in Libya (AAPC: 2.1277 [95% CI: 2.0275 to 2.2279, $p = 0.000$]), while the fastest declining rate was in Italy (AAPC: −1.9313 [95% CI: −2.0741 to −1.7882, $p = 0.000$]).

The highest incidence rates of MS among the 10–24 years age group in 2021 were observed in Greenland (6.73, 95% CI: 5.74 to 7.77), followed by Sweden (5.41, 95% CI: 3.79 to 7.35) and Ireland (4.39, 95% CI: 2.78 to 6.45). The fastest-growing incidence rate of MS was in Taiwan (AAPC: 3.676 [95% CI: 3.5203 to 3.832, $p = 0.000$]), while the fastest declining rate was in the Northern Mariana Islands (AAPC: −0.2799 [95% CI: −0.5068 to −0.0526, $p = 0.015837$]).

Correlation analysis between SDI and incidence rate

To explore the factors behind the changes in incidence rates, we conducted a correlation

Fig. 5 Incidence rate of asthma (A), AD (B), Psoriasis (C), diabetes (D), RA (E), IBD (F) and MS (G) for 204 countries and territories in 2021 by SDI. The black line represents the expected prevalence rate based solely on SDI. Locations lower than the solid black line had a lower-than-expected burden, while those below the line had a lower-than-expected burden. YLDs: Years Lived with Disability, AD: Atopic Dermatitis, RA: Rheumatoid Arthritis, MS: Multiple Sclerosis, IBD: Inflammatory Bowel Disease, SDI: Socio-Demographic Index



analysis between incidence rates and the SDI (Fig. 5). We found that, except for asthma, there is a certain correlation between the incidence of other diseases and the SDI. Higher SDI is associated with higher incidence rates, showing a positive correlation, especially for AD and psoriasis. Additionally, developed countries in Europe and North America showed higher incidence rates at the same SDI level, which is worth further consideration.

Comparison of concentration index and slope index of YLDs in 1990 and 2021

To further study the population concentrated with disease burden, we calculated the concentration index and slope index (Supplementary Table 6, Fig. 6). Interestingly, the absolute burden of YLDs for the 7 diseases was concentrated in high SDI regions, consistent with our correlation analysis. Particularly for IBD and MS, the concentration indices in 2021 were −0.276 and −0.363, respectively, showing a significant improvement from −0.409 and −0.424 in 1990. Furthermore, the slope index indicated that the higher the SDI, the higher the YLDs rate. The gap in YLDs rates among different SDI levels for diabetes, MS, and RA has widened in 2021 compared to 1990, which warrants further investigation into the influencing factors.

DISCUSSION

IMIDs form a class of chronic inflammatory diseases caused by immune imbalance, affecting multiple organs and tissues.[20] IMIDs include various autoimmune diseases, such as asthma, AD, psoriasis, RA, diabetes, MS, IBD, and systemic lupus erythematosus, covering multiple age groups.[1] Previous research has found that the 10–24 age group is one of the high-risk groups for various IMIDs.[4] Due to the lack of effective curative treatments for IMIDs, they are also the group that suffers the longest. Additionally, younger people are one of the most

Fig. 6 Concentration curves and cross-country inequality regression curves for the YLDs of asthma (A, B), AD (C, D), Psoriasis (E, F), diabetes (G, H), RA (I, J), IBD (K, L) and MS (M, N) worldwide, 1990 and 2021. YLDs: Years Lived with Disability, AD: Atopic Dermatitis, RA: Rheumatoid Arthritis, MS: Multiple Sclerosis, IBD: Inflammatory Bowel Disease

vulnerable groups in society, especially after the COVID-19 pandemic. Therefore, the burden on individuals aged 10–24 with IMIDs, as well as the burden IMIDs place on society, are substantial. Based on this, we utilized the latest GBD 2021 data to analyze the spatiotemporal differences in IMIDs among the global 10–24 age group to identify the incidence characteristics of IMIDs in this age group, providing suggestions for more targeted health policies and preventive measures.

First, we conducted a preliminary exploration of the incidence rate changes of 7 types of IMIDs from 1990 to 2021 and found that asthma, AD, and psoriasis had the highest incidence rates, while MS had the lowest. This is consistent with the global age-standardized incidence rate distribution. Secondly, we investigated the gender differences in these 7 diseases and interestingly found that compared to males, females had significantly higher incidence rates of asthma, AD, psoriasis, RA, and MS. Previous studies have also reported gender differences in IMIDs, suggesting that these differences may be caused by factors such as organ function, sex hormones, and gut microbiota.

Estrogen can enhance immune responses under normal circumstances, but it has the opposite effect in RA and other rheumatic autoimmune diseases.[27] Androgens can negatively regulate type 2 innate lymphoid cells and reduce the activation of dendritic cells, thereby mitigating immune responses.[28] AD and IBD are more common in boys during childhood, but the incidence is higher in females during adolescence.[29,30] This reversal is likely due to hormonal changes during puberty, especially the immune-enhancing effect of estrogen and the immunosuppressive effect of androgens.[27] Additionally, sex hormones may influence AD development and progression by altering skin immune responses and skin barrier function.[30] The incidence rate of IBD peaks during adolescence, with approximately 25% of patients being diagnosed with IBD before the age of 18.[29] The highest incidence rates of Crohn's disease and ulcerative colitis are in the 15 to 17.9 age group, further indicating that hormones may play a role in the development of IMIDs.[29] Most interestingly, psoriasis progression is influenced by menstruation, pregnancy, and menopause.[31] Estrogen can inhibit the activity of pro-inflammatory cytokines and stimulate Th2 cells to produce anti-inflammatory molecules, promoting the conversion of T cells to regulatory T cells, thereby negatively regulating immune responses and alleviating psoriasis symptoms.[30]

Next, we used joinpoint regression analysis to explore the temporal differences in the incidence rates and YLDs of IMIDs. The results showed that compared to 1990, the incidence rates of asthma and AD significantly decreased, while the incidence rates of psoriasis, RA, and diabetes significantly increased, with YLDs showing the same trend. This indicates that we may need to pay more attention to the prevention and management of psoriasis, RA, and diabetes in adolescents. Specifically, we found that the incidence rates and YLDs of psoriasis and diabetes showed a significant upward trend after 2019, while AD and RA showed a downward trend. The year 2019 marked the beginning of the COVID-19 pandemic, followed by the global outbreak in 2020. The relationship between IMIDs and COVID-19 has been controversial.[32] Previous reports indicated that COVID-19 patients developed or relapsed an IMID after infection.[3] After COVID-19 infection, IFN is activated, triggering immune responses and leading to chronic inflammation.[33] The COVID-19 virus stimulates the transformation of Th17 and Th2 cells, with Th17 being crucial in the development of psoriasis and Th2 in activating IBD. COVID-19 also increases the risk of type 1 diabetes and RA,[33] which aligns with our findings. Additionally, some reports suggest that COVID-19 vaccination increases the risk of developing IMIDs, although this has been disproved in some literature.[34,35]

Then, we analyzed the incidence of IMIDs in the 10–24 age group at the national level and examined its association with the SDI. We calculated the concentration index and slope index to explore the distribution patterns. Our findings show that IMIDs are predominantly prevalent in Western Europe and North America, which is consistent with previous research.[4]

Our data analysis cannot fully explain the distributional differences of IMIDs. However, based on previous studies, we can propose potential

factors that may influence the incidence of IMIDs. First is genetic susceptibility;[20,36] the majority of IMID patients carry susceptible genes, and some of these genes are found predominantly in Western Europe and North America, but are rare in Asian populations, directly causing spatial differences in incidence rates.[20] Secondly, environmental factors play a crucial role.[37] Living in urban areas and exposure to high emissions and elevated PM2.5 levels are significant risk factors for RA.[38] The availability of green spaces in residential areas is correlated with the incidence of IMIDs.[37] Dust exposure is associated with an increased risk of asthma and AD.[39] Thirdly, dietary habits have been linked to the development of IMIDs.[40,41] Fourth, and equally important, is the role of infections, which are strongly associated with IMIDs.[42] For instance, after contracting COVID-19, the risks of psoriasis, RA, and diabetes increase.[43] Epstein-Barr virus has been identified as a risk factor for both RA and MS.[44,45] Skin infections, including parasitic infections, can trigger AD.[46] Importantly, the hygiene hypothesis was initially described in relation to allergic diseases and was later extended to autoimmune diseases in the early 2000s.[47] It suggests that infections may play a protective role in reducing the incidence of autoimmune diseases.[47] For instance, broadly speaking, the frequency of infections is negatively correlated with the incidence of autoimmune diseases.[48] The incidence rate of type 1 diabetes in a population is inversely correlated with the incidence rate of tuberculosis.[49] Patients undergoing anti-parasitic treatments have shown worsened asthma symptoms, while infection with live parasites such as *Trichuris suis* has demonstrated beneficial effects in patients with multiple sclerosis.[48] The hypothesis further posits that the gut microbiome may influence autoimmune diseases.[48] Although the hypothesis itself remains controversial and has even been challenged, it offers a novel perspective on explaining differences in the incidence rates of IMIDs. In regions with high SDI, elevated hygiene standards result in lower infection rates, which in turn may lead to higher IMID incidence rates. This is a plausible and intriguing hypothesis. However, our analysis failed to explore the factors affecting the distribution of IMIDs, which needs to be further explored in the future.

Interestingly, it is worth noting that subsequent joinpoint regression analysis indicates that South America and Asia, especially China, show high AAPC, suggesting that IMID incidence rates are quietly rising in these regions. SDI reflects the level of socio-economic development in a region and its impact on health outcomes, highlighting disparities in disease burden, health risks, and transitions in health trends across different development stages.[50] SDI correlation analysis and cross-regional inequity analysis further indicate that the burden of IMIDs is concentrated in high-SDI regions, particularly for MS and IBD. Compared to 1990, although most IMIDs show regional consistency, high-SDI regions still face higher risks. While focusing on high-incidence regions, we must also pay attention to the incidence of IMIDs in emerging regions such as Asia and South America. Only in this way can we effectively reduce the heavy burden that IMIDs place on young people globally. It is worth noting that the healthcare systems, and the accessibility and quality of healthcare vary across nations. Nations with high healthcare accessibility and advanced medical systems may exhibit higher IMID diagnosis rates, more comprehensive medical reporting systems, and higher reporting rates, resulting in elevated reported incidence rates. These factors may warrant further investigation; however, they fall outside the scope of this study.

The strength of this study lies in its utilization of the latest GBD 2021 data, employing joinpoint regression, SDI correlation analysis, and inter-regional equity methods to comprehensively elucidate the global incidence differences of IMIDs among the 10–24 age group from a temporal and spatial perspective. Through these analyses, it reveals the patterns of IMID incidence among young populations, providing robust data support for the development of targeted health governance policies.

However, the study also has its limitations. Firstly, the GBD 2021 data relies on voluntary reporting from countries, which may lead to potential underestimation and data biases. Secondly, in the SDI correlation analysis, factors outside of SDI were not considered, introducing uncertainty regarding the relationship between SDI and incidence rates. Moreover, although SDI is a composite indicator, it cannot directly reflect the healthcare and economic levels of a country or

region, which may consequently introduce bias. Additionally, demographic data sourced from the United Nations website and disease-related data from GBD 2021 may differ in estimation methods, affecting the slope index and concentration index. Future research should meticulously consider data sources and methodological choices to enhance the accuracy and reliability of analyses. Recognizing that our current analysis solely explores the correlation between SDI and incidence rates without addressing potential confounders, future research will prioritize investigating the drivers of regional variations in IMID incidence. By integrating data from diverse databases and systematically adjusting for confounding factors such as healthcare accessibility, diagnostic capacity, urbanization levels, and environmental quality indices, we aim to identify and elucidate the key risk factors underlying IMID development. In addition, given that our study focuses on time series data, we will incorporate fixed-effects or multilevel models to address potential biases arising from differences across countries in the analysis in the future.

CONCLUSION

The burden of IMIDs in adolescents aged 10–24, ranked by severity, includes asthma, AD, psoriasis, diabetes, RA, IBD, and MS. Among these, asthma, AD, psoriasis, RA, and MS are more prevalent in females. Compared to 1990, the incidence rates of asthma and AD decreased in 2021, while the rates of psoriasis, diabetes, and RA increased. IMIDs are more common in Western Europe and North America, with rising incidence rates in South America and Asia. These diseases are primarily concentrated in high SDI regions, although the incidence rate differences between countries are decreasing.

Abbreviations

IMID, Immune-Mediated Inflammatory Disease; AD, Atopic Dermatitis; RA, Rheumatoid Arthritis; MS, Multiple Sclerosis; IBD, Inflammatory Bowel Disease; GBD, Global Burden of Disease; AAPC, Average Annual Percentage Change; SDI, Socio-Demographic Index.

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Availability of data and materials

The data is available in the 2021 Global Burden of Disease study (healthdata.org). Joinpoint software could be downloaded at Download Joinpoint Software (cancer.gov). Demographic data sourced from the United Nations (https://population.un.org/wpp/).

Author contributions

XL, HX and BY designed and conducted the whole research. KL, YD, ZWZ and YW revised and finalized the manuscript.

Authors' consent for publication

All authors unanimously agree to submit the manuscript for publication.

Declaration of competing interest

The authors declare they have no conflict of interest.

Ethics approval

Not applicable.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2025.101033.

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