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Original Communication

Global Burden of Diseases Associated With Iron Deficiency: GBD 2021

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Abstract

Background: Iron deficiency is a major global public health concern associated with various adverse outcomes. **Methods**: This study utilized the Global Burden of Disease Study 2021 (GBD 2021) to analyze the contemporary burden of iron deficiency-associated diseases. We conducted an epidemiological analysis using Bayesian age-period-cohort methods for forecasting, decomposition analysis to assess the impact of aging, population growth, and epidemiological shifts, and slope/concentration indices to assess health inequalities. **Results**: Between 1990 and 2021, disability-adjusted life years (DALYs) due to iron deficiency increased (2021: 34,519,623, 95% uncertainty interval [UI]: 23,607,706.06–48,762,323.14), despite a decline in age-standardized rates (ASR) (451.58 per 100,000; 95% UI: 308.48–639.42) with an estimated annual percentage change of –0.87 (95% confidence interval [CI]: –0.91 to –0.83). The burden was highest in low socio-demographic index regions, with 13,893,312.7 DALYs (95% UI: 9,567,547.98–19,440,905.71), an ASR of 735.34 per 100,000 (95% UI: 506.01–1027.57), and an annual percentage change (EAPC) of –1.36 (95% CI: –1.41 to –1.32). Deaths totaled 18,628.31 (95% UI: 9082.46–27,243.01), with a mortality rate of 1.77 per 100,000 (95% UI: 0.86–2.60), primarily from maternal health disorders and dietary iron deficiency. Population growth and epidemiological shifts were key contributors to the disease burden. **Conclusions**: These findings highlight the persistent global burden of iron deficiency and the need for targeted interventions, particularly in low socio-demographic index regions.

Keywords: iron deficiency; global health; epidemiology; maternal diseases; nutritional diseases

1. Introduction

Iron deficiency is a prevalent global public health concern linked to various adverse health outcomes [1–3]. The Global Burden of Disease Study 2021 (GBD 2021) identifies multiple diseases associated with iron deficiency [4,5]. These include maternal complications such as sepsis, hemorrhage, hypertensive disorders, obstructed labor and uterine rupture, ectopic pregnancy, maternal deaths aggravated by Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS), as well as dietary iron deficiency [3,6,7].

Prior research has delineated the impact of iron deficiency on maternal mortality and nutritional deficiencies. It is associated with an increased risk of gestational hypertension, preterm birth, low birth weight, developmental delays, and cognitive impairments in neonates [8–11]. Beyond its direct health effects, iron deficiency imposes a significant economic burden globally [12,13]. Annually, iron deficiency causes significant economic costs, including healthcare expenses, productivity losses, and reduced quality of life [14,15]. Estimating the economic toll is challenging owing to differences in methodologies and data availability; however, evidence suggests it is considerable [16]. Addressing the economic impact of iron deficiency is crucial for effective public health strategies worldwide [17].

This study provides an up-to-date analysis of the global disease burden associated with iron deficiency using the 2021 GBD data. The study elucidates the current disease burden, examines trends over time, and assesses regional health disparities, aging effects, population growth, and epidemiological shifts. We hypothesize that the global burden of iron deficiency-related diseases has evolved, thereby showing regional differences driven by demographic shifts, including aging, population growth, and epidemiological changes. This research is crucial for informing public health policies and interventions to mitigate the impact of iron deficiency on global health.

2. Materials and Methods

2.1 Data Source

Data for this study were obtained from GBD 2021, which provides comprehensive and standardized estimates of health outcomes. The GBD estimate column was utilized, focusing on the "risk factor" definition to analyze iron deficiency as a determinant. The selected diseases associated with this risk factor primarily included maternal health disorders and malnutrition-related conditions, such as iron deficiency anemia. The Institutional Review Board of the University of Washington reviewed and approved a consent waiver for the GBD research.

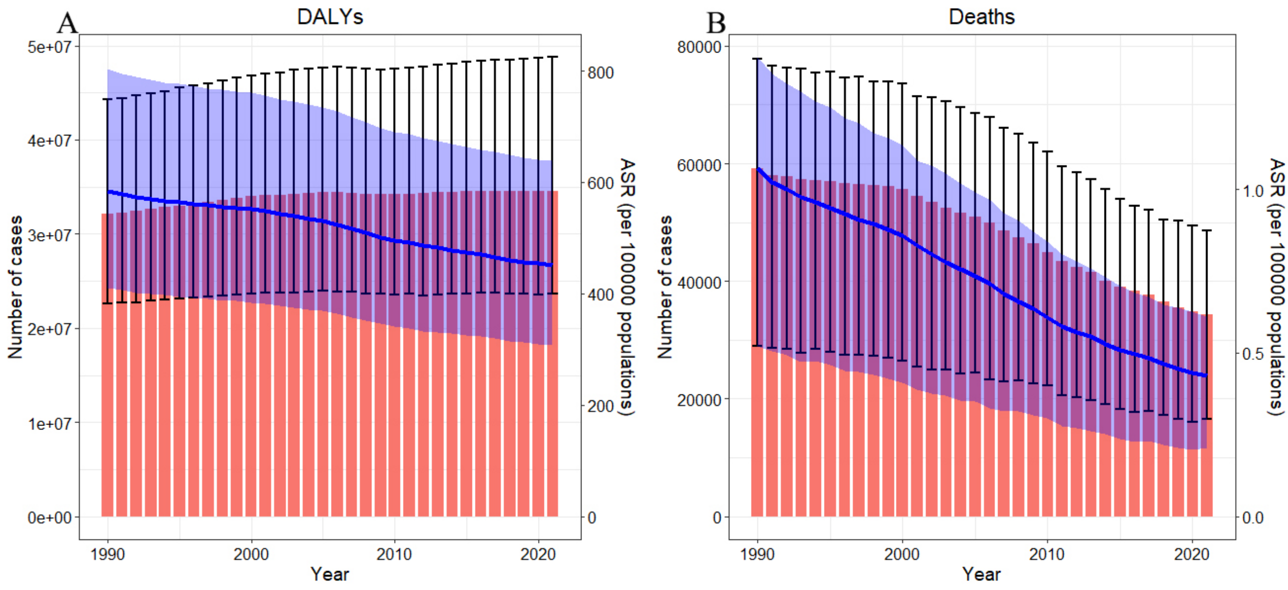

Fig. 1. Bar and line charts of the global burden of diseases by iron deficiency from 1990 to 2021. (A) Bar and line charts of DALYs regarding the number of cases and ASRs, respectively. (B) Bar and line charts of the associated mortality regarding numbers and ASRs, respectively. Error bar and line represent its 95% uncertainty interval. ASR, age-standardized rates; DALYs, disability-adjusted life years.

2.2 Measurements and Stratification

In this study, multiple health metrics were assessed, including disability-adjusted life years (DALYs) and deaths, using both rate and absolute numbers as indicators. The analysis was stratified by sex, location (global, five socio-demographic index [SDI] quintiles, GBD super regions—including high-income, Southeast Asia, East Asia, and Oceania; South Asia; Central Europe, Eastern Europe, and Central Asia; North Africa and the Middle East; Latin America and the Caribbean; and Sub-Saharan Africa—as well as 204 individual countries and territories), age (categorized as all ages, age-standardized, and 5-year age groups from 0–95+ years), various diseases attributable to iron deficiency as a risk factor, and the statistical period between 1990 and 2021.

2.3 Analytical Approaches

First, we conducted a comprehensive epidemiological analysis of GBD associated with iron deficiency. We also forecasted the burden of disease due to iron deficiency risk factors up to 2030 using Bayesian age-period-cohort (BAPC) methods. To assess the robustness of the model, we performed a sensitivity analysis by sex. Additionally, we calculated the annual percentage change (EAPC) between 1990 and 2021. Second, we constructed pyramid graphs to visualize the distribution of various disease types associated with iron deficiency risk factors across age groups and sexes, including maternal health disorders and dietary iron deficiency. Subsequently, we created world maps to illustrate the changes in DALYs and deaths between 1990 and 2021, as well as regional and national differences. These maps included overall disease burden maps for iron deficiency risk factors and specific disease burden maps for 2021. Fourth, we employed the joinpoint model to identify three inflection points from 1990 to 2021 in the age-standardized rates (ASR) of DALYs and deaths due to iron deficiency risk factors. We calculated the slopes of linear models before and after each inflection point. Fifth, we decomposed the analysis to explore the contributions of overall difference, aging, population, and epidemiological change to the disease burden at the global level, across SDI quintiles, and GBD-defined super regions. This analysis provided insights into the underlying causes of disease prevalence in different areas. Sixth, we conducted a health inequality analysis using slope and concentration indices to assess the ASR of DALYs across 204 countries and territories in 1990 and 2021. This analysis included linear and robust regression slopes and intercepts, heteroscedasticity tests for linear regression to control the risk of false positives, and slope and concentration indices with their standard deviations (SE) and *p*-values.

2.4 Statistical Analysis

All statistical computations and graphical illustrations were performed using R software (version 4.4.1, R Foundation for Statistical Computing, Vienna, Austria), except for the concentration index, which was calculated using the "*conindex*" package in Stata/MP (64-bit, version 17, StataCorp LLC, TX, USA). Data manipulation and filtering were conducted with the "*tidyverse*", "*foreign*", and "*data.table*" packages. Visualizations were created using "*ggbrace*", "*ggplot2*", "*ggsci*", "*ggrepel*", and "*patchwork*". For robust regression analysis of the slope index and fitting heteroscedastic and functional models, we employed the "*MASS*", "*car*", "*splines*", "*broom*", and "*mgcv*" packages. Statistical significance was set at a *p*-value of less than 0.05.

3. Results

3.1 Global Burden, Trend, and Projections

Globally, between 1990 and 2021, the number of DALYs attributed to iron deficiency risk factors gradually increased, reaching 34,519,623 in 2021 (95% uncertainty interval [UI]: 23,607,706.06–48,762,323.14). Conversely, the ASR of DALYs showed a slight decline, which dropped to 451.58 per 100,000 population (95% UI: 308.48–639.42), with an EAPC of –0.87 (95% confidence interval [CI]: –0.91 to –0.83) (Fig. 1, **Supplementary Table 1**).

Projections for 2030 indicate a continued increase in the absolute number of DALYs, reaching 34,949,009.93 (95% UI: 29,108,251.59–40,789,768.27), whereas the ASR is expected to decline further to 427.25 per 100,000 population (95% UI: 353.77–500.73) (**Supplementary Fig. 1**, **Supplementary Table 1**).

Regarding mortality risk, the number of deaths in 2021 had decreased to approximately one-third of the 1990 level, thus reaching 34,291.78 (95% UI: 16,601.2–48,547.65). The ASR declined significantly to 0.43 per 100,000 population (95% UI: 0.21–0.61), with an EAPC of –2.98 (95% CI: –3.09 to –2.87) (Fig. 1, **Supplementary Table 2**).

3.2 Burden of Different Diseases and Age Groups in 2021

This section presents a stratified analysis of the burden of diseases associated with iron deficiency across different age groups and sexes. Our analysis of global DALY pyramids revealed that dietary iron deficiency, which causes iron-deficiency anemia, was the predominant contributor to the burden, with a total of 32,315,750.9 DALYs (95% UI: 21,779,579.62–46,496,969.19) and a rate of 423.74 per 100,000 population (95% UI: 285.27–610.83). This burden was particularly pronounced in the $<$5 age group (DALYs: 5,735,700.11, 95% UI: 3,855,780.51–8,345,160.53; rate: 871.46 per 100,000 population; 95% UI: 585.83–1267.93), the 5–9 age group (DALYs: 4,118,696.95, 95% UI: 2,674,561.75–6,120,200.41; rate: 599.47 per 100,000 population; 95% UI: 389.28–890.79), and the $\geq$95 age group (DALYs: 39,803.67, 95% UI: 26,615.55–57,353.24; rate: 730.3 per 100,000 population, 95% UI: 488.33–1052.29) (Fig. 2A,B, **Supplementary Table 1**).

Among reproductive-aged women, maternal hemorrhage was the most severe maternal disorder linked to iron deficiency, with 531,056.59 DALYs (95% UI: 259,030.04–759,994.05) and a rate of 6.73 per 100,000 population (95% UI: 3.28–9.63). Maternal hypertensive disorders ranked second, with 442,628.3 DALYs (95% UI: 212,292.32–630,005.47) and a rate of 5.61 per 100,000 population (95% UI: 2.69–7.98) (Fig. 2A,B, **Supplementary Table 1**).

For mortality burden, the 20–24 and 25–29 age groups faced the highest risk of death due to iron deficiency, with 6581.16 deaths (95% UI: 3156.62–9196.17) and 6557.04 deaths (95% UI: 3131.24–9345.24), respectively. The mortality rates for these age groups were 1.1 (95% UI: 0.53–1.54) and 1.11 (95% UI: 0.53–1.59) per 100,000 population.

Beyond age-specific mortality, maternal hemorrhage was also significantly impacted. Maternal hemorrhage accounted for 8426.43 deaths (95% UI: 4085.41–12,172.75), with a mortality rate of 0.11 per 100,000 population (95% UI: 0.05–0.15). Similarly, maternal hypertensive disorders resulted in 6846.71 deaths (95% UI: 3285.04–9813.78), which corresponded to a mortality rate of 0.09 per 100,000 population (95% UI: 0.04–0.12) (Fig. 2C, **Supplementary Table 2**).

3.3 Burden and Trends by Regions and 204 Countries or Territories

In 2021, the region with the lowest burden, characterized by high SDI, reported 791,204.49 DALYs cases (95% UI: 523,259.19–1,167,818.65), with an ASR of 73.37 per 100,000 population (95% UI: 48.39–109.59) and an EAPC of –0.92 (95% CI: –1.05 to –0.8) between 1990 and 2021 (**Supplementary Table 1**). Conversely, the region with the highest burden, identified as low SDI, recorded 13,893,312.7 DALY cases (95% UI: 9,567,547.98–19,440,905.71), an ASR of 735.34 per 100,000 population (95% UI: 506.01–1027.57), and an EAPC of –1.36 (95% CI: –1.41 to –1.32) (**Supplementary Table 1**).

Similarly, South Asia experienced an immense burden, with 16,226,512.16 DALYs cases (95% UI: 11,153,720.17–23,108,620.08), an ASR of 912.28 per 100,000 population (95% UI: 627.82–1298.36), and an EAPC of –1.4 (95% CI: –1.44 to –1.35), thus suggesting a declining disease burden (Fig. 3A,C,E, **Supplementary Table 1**).

Regarding deaths attributed to iron deficiency, the low SDI region bore the highest burden in 2021, with 18,628.31 deaths (95% UI: 9082.46–27,243.01) and an ASR of 1.77 per 100,000 population (95% UI: 0.86–2.60) (**Supplementary Table 2**). Similarly, South Asia faced a severe impact, with 8292.81 deaths (95% UI: 3921.69–11,613.58) and an ASR of 0.40 per 100,000 population (95% UI: 0.19–0.56).

These findings highlight the significant burden in these regions, with EAPCs of –3.02 (95% CI: –3.21 to –2.82) for the low SDI region and –6.08 (95% CI: –6.38 to –5.78) for South Asia, thus indicating a declining burden between 1990 and 2021 (Fig. 3B,D,F, **Supplementary Table 2**). Maps depicting the overall trends in DALYs, deaths, and ASRs across 204 countries and territories in 1990 are provided in **Supplementary Fig. 2**. The global burden dis-

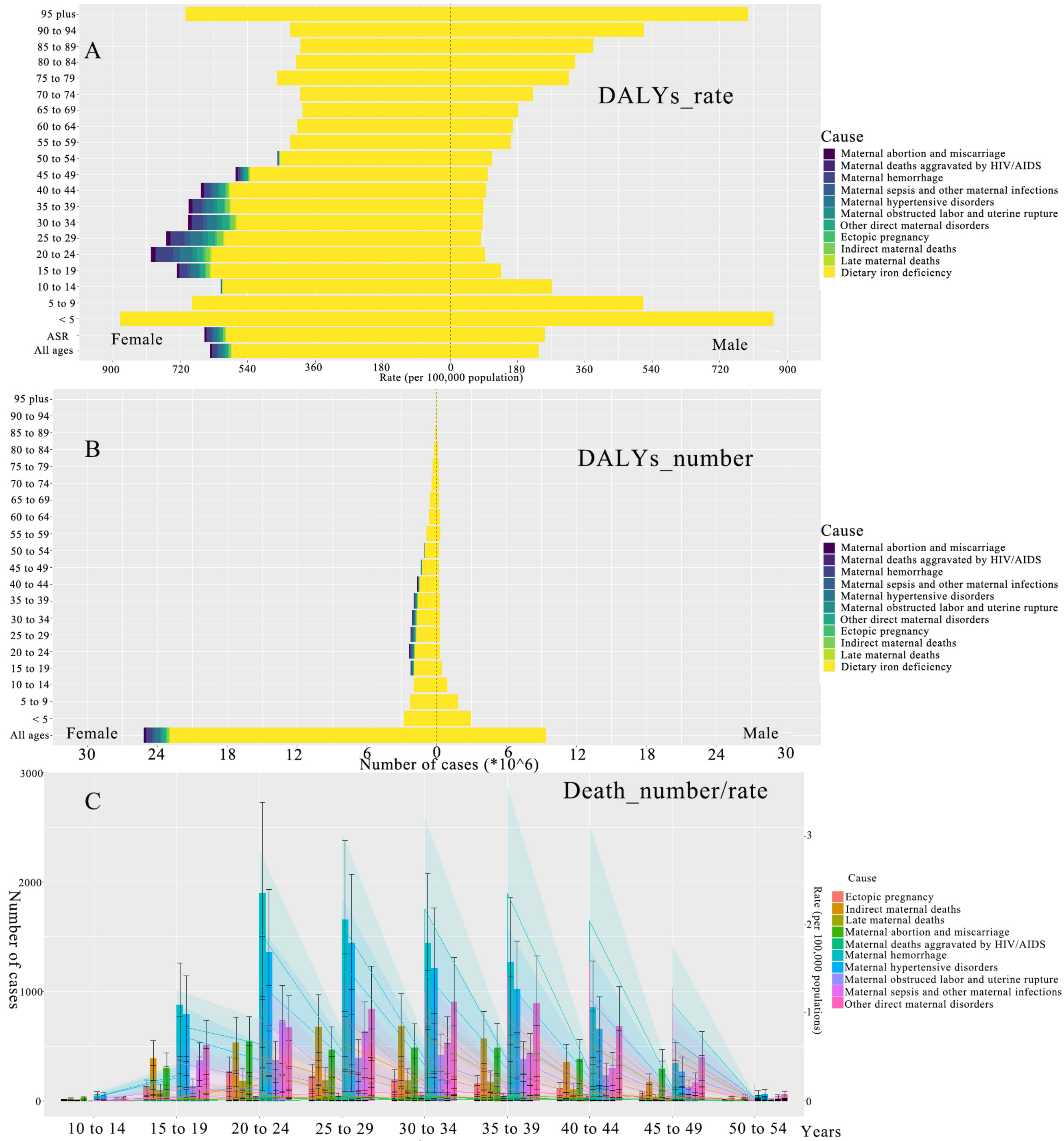

Fig. 2. Sex-differentiated age-specific distribution of the diseases by iron deficiency. (A) The graph shows the DALYs regarding the ASR. (B) The graph shows the DALYs regarding case numbers. (C) Bar and line charts of the associated mortality by diseases regarding numbers and ASRs, respectively. Error bar and line represent its 95% uncertainty interval. DALYs, disability-adjusted life years; ASR, age-standardized rates.

tributions for the remaining 11 diseases caused by iron deficiency are present in **Supplementary Figs. 3–13**.

3.4 Joinpoint Model

To delineate the temporal dynamics between 1990 and 2021 and to address the limitations of conventional linear models, which assume a single trend over the entire period, we employed the joinpoint regression model to segment the timeframe into four distinct intervals. Regarding the ASR of DALYs (Fig. 4A), the average annual percentage change (AAPC) was –0.82, thus indicating a gradual decline from 1990 to 2002, with an annual percentage change (APC) of

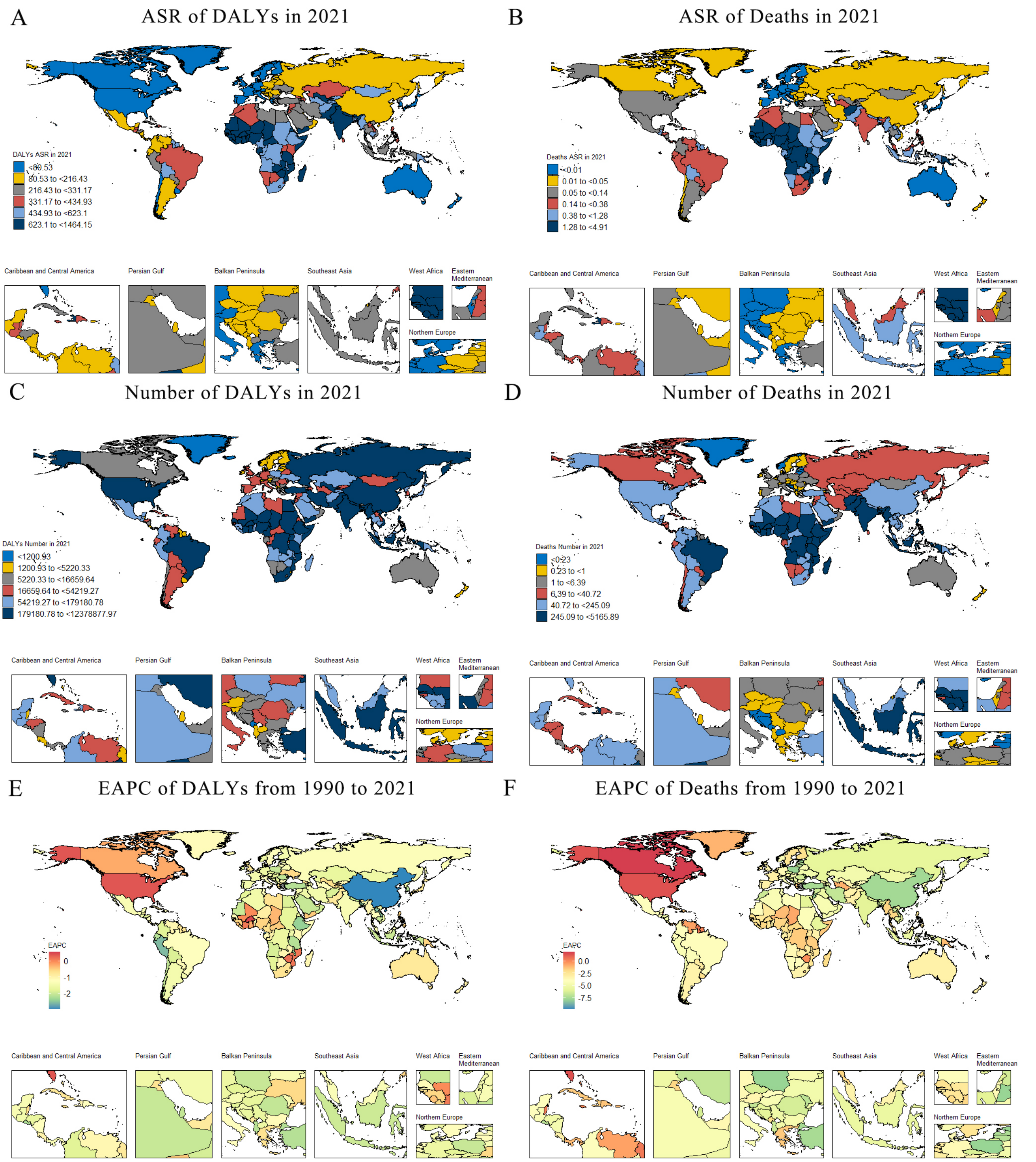

Fig. 3. Global distribution maps of the burden of diseases by iron deficiency in 204 countries and territories. (A) The DALYs regarding the ASR in 2021. (B) The deaths regarding the ASR in 2021. (C) The DALYs regarding the number in 2021. (D) The deaths regarding the number in 2021. (E) The DALYs of the EAPC from 1990 to 2021. (F) The deaths regarding the EAPC from 1990 to 2021. DALYs, disability-adjusted life years; ASR, age-standardized rates; EAPC, estimated annual percentage change.

–0.55. Subsequently, the decline steepened, thus reaching –0.89 in 2006 and –1.58 in 2009. Between 2009 and 2021, the rate of decrease moderated, with an APC of –0.88. Regarding the ASR of deaths (Fig. 4B), the APC was –2.83. A gradual decline occurred between 1990 and 2000 (APC = –1.98), followed by sharper reductions until 2006 (APC = –3.08) and 2009 (APC = –3.69). Between 2009 and 2021, the decline slowed, with an APC of –2.83. APCs and AAPCs in different SDI regions are summarized in **Supplementary Fig. 14**.

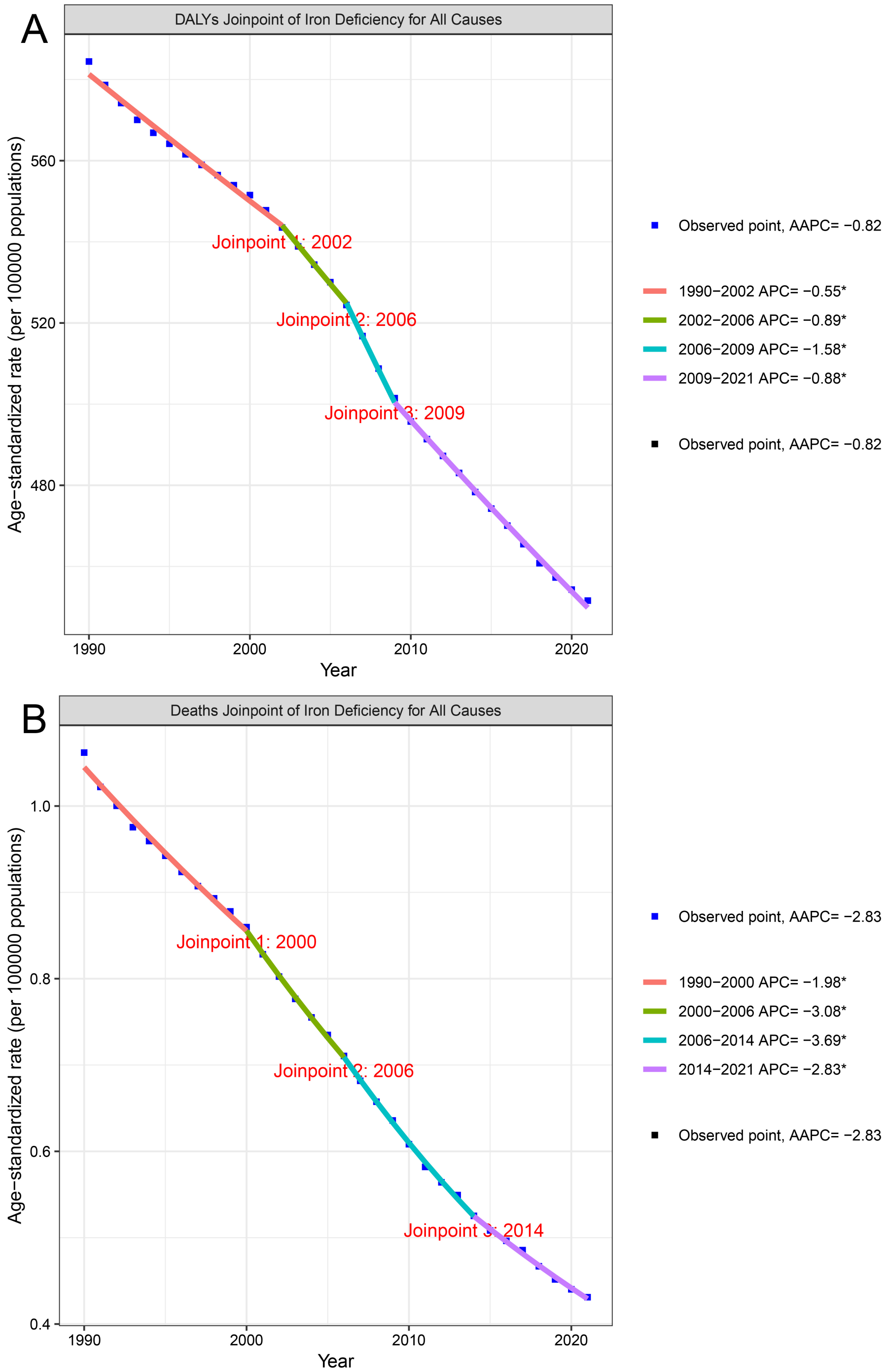

Fig. 4. Joinpoint modeling of the burden of diseases by iron deficiency from 1990 to 2021, with the AAPCs and the four segments' APCs. (A) Changes over time based on the DALYs model. (B) Changes over time based on the deaths model. AAPC, average annual percent change; APC, annual percent change; DALYs, disability-adjusted life-years.

3.5 Decomposition Analysis

The decomposition analysis elucidates the contributions of aging, population growth, and epidemiological change to changes in DALYs (Fig. 5A) and deaths (Fig. 5B) due to iron deficiency between 1990 and 2021 (**Supplementary Table 3**). Globally, the net change in DALYs was 2,360,395.79, primarily driven by population growth (13,295,630.12) and counterbalanced by epidemiological change (–8,897,507.32). Aging (–2,037,727.02) also contributed significantly. Notably, the region with the most substantial overall difference was Sub-Saharan Africa, with an increase of 3,543,719.77 DALYs, largely driven by population growth (6,643,515.22) and offset by negative contributions from epidemiological change (–2,988,591.23) and aging (–111,204.22). Globally, deaths

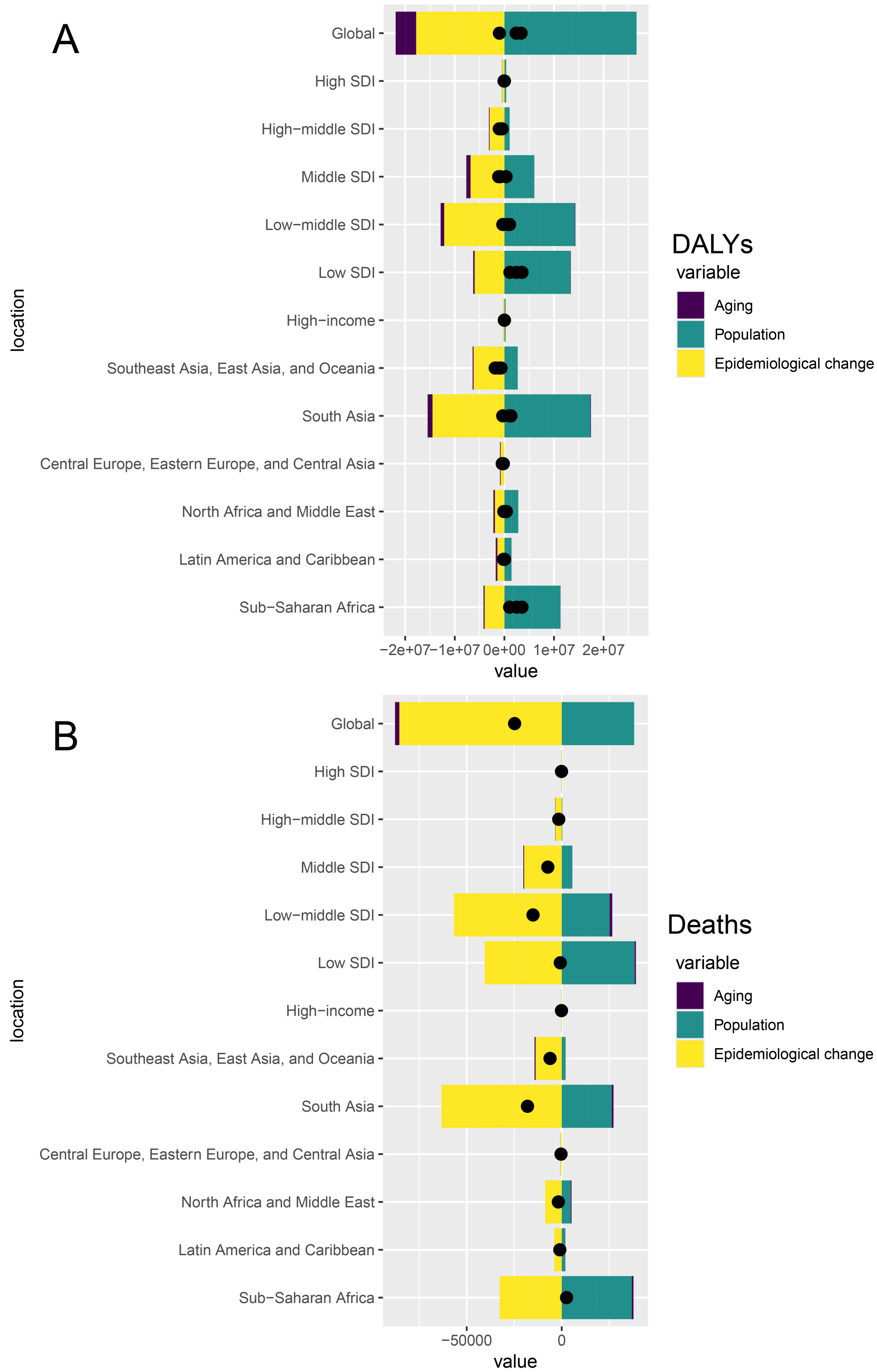

Fig. 5. Changes in the burden of diseases by iron deficiency according to population-level determinants (population growth, aging, and epidemiological changes) from 1990 to 2021 at the global level based on five SDI quintiles and seven GBD-defined super-regions. (A) DALYs rate. (B) Mortality rate. In all panels, the black dots represent the overall value of the change based on the contribution of all three components. SDI, Sociodemographic Index; DALYs, disability-adjusted life years.

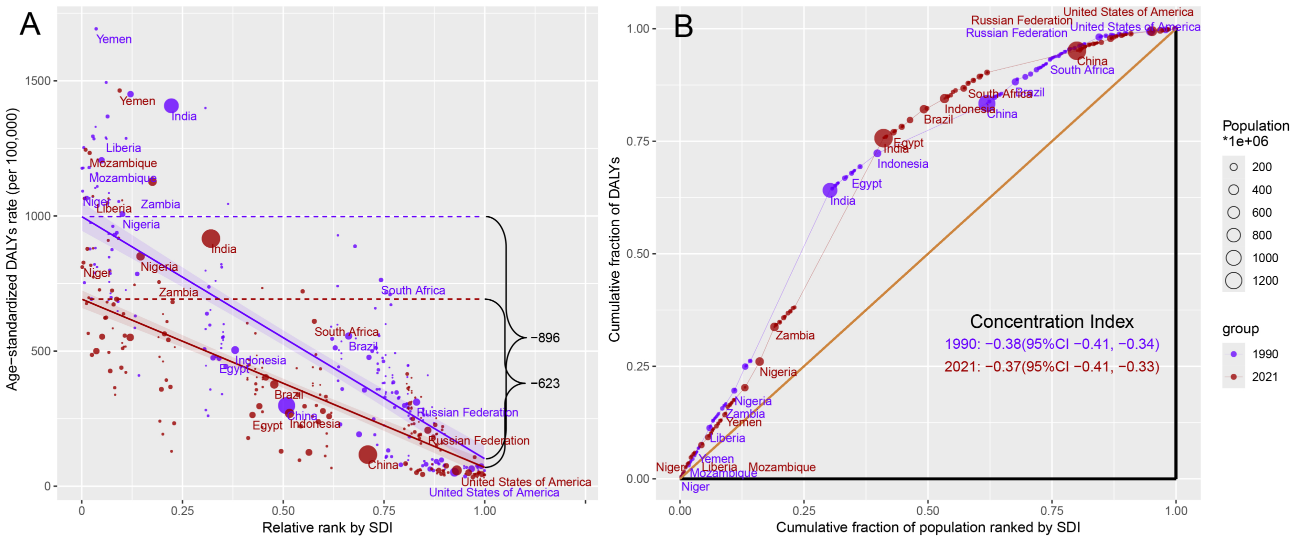

Fig. 6. Assessment of the global health inequality related to diseases by iron deficiency. (A) Slope indices of inequality based on the DALYs in 1990 and 2021 (the numbers adjacent to the brackets indicate the slopes). (B) Concentration indices of inequality based on the DALYs in 1990 and 2021. (In both panels, each country or region is represented by a solid dot, with larger dots indicating a higher population). SDI, Socio-demographic Index; ASR, age-standardized rate.

decreased by 24,791.75, primarily caused by epidemiological change (–42,729.53), followed by population growth (19,042.71), whereas aging made a minor positive contribution (1104.94). Sub-Saharan Africa saw the largest increase in (2562), primarily driven by epidemiological change (–16,224.05), partially offset by population growth (18,368.43) and a minor positive effect from aging (417.62).

3.6 Global Health Inequalities Analysis

Health inequality, assessed through the slope and concentration indices of the ASR for deaths and DALYs due to iron deficiency, highlights significant disparities across SDI levels and regions. Globally, between 1990 and 2021, ASR for DALYs declined, which indicated a positive trend in reducing the burden of iron deficiency. However, the slope indices show that the rate of decrease varied over time, with more pronounced reductions in earlier years (Fig. 6A). The concentration indices further suggest increasing disparities, as more negative scores reflect greater health inequality (Fig. 6B). Disparities are particularly pronounced in low-SDI regions (**Supplementary Tables 4–6**). For deaths, the slope index in 2021 was –2.38 (95% CI: –3.28 to –1.49, lm, p = 0.0059), which reflected a steeper reduction compared to the global average. The concentration index for deaths in low SDI regions was –0.1567 (95% CI: –0.2371 to –0.0762), suggesting a widening gap in iron deficiency-related health outcomes. Similarly, for DALYs in 2021, the slope index was –281.17 (95% CI: –566.02 to 3.68, rlm, p = 0.0807), and the concentration index was –0.0302 (95% CI: –0.106 to 0.0456), thus increasing health inequality in these regions.

4. Discussion

The study highlights the significant global burden of iron deficiency-related diseases, which remain a pressing public health issue. A comprehensive analysis of the GBD 2021 data revealed that although ASRs of DALYs and deaths due to iron deficiency have slightly declined, the absolute number of cases has increased, thereby highlighting the impact of population growth and aging on disease burden. Reducing the burden of iron deficiency-related diseases yields significant social and economic benefits. Mitigating iron deficiency can improve quality of life, reduce healthcare costs, and enhance productivity, which ultimately benefit societies worldwide.

Iron deficiency persists as a significant global health challenge, with absolute fatalities and DALYs increasing despite a decline in age-standardized mortality and DALY rates between 1990 and 2021. Population growth and epidemiological shifts are key drivers of the changing burden of iron deficiency-related diseases. This pattern is particularly evident in low- and middle-income countries, where iron deficiency and iron deficiency anemia have a significant impact on the health of children and expectant women [18,19]. Research has demonstrated that iron deficiency impairs physical health and negatively affects cognitive function and psychological development, especially in children <7 [20,21]. In India, inadequate iron intake is a critical concern, with forecasts indicating that rising carbon dioxide levels may reduce iron bioavailability and potentially increase the population at risk of deficiency [22–24]. Although certain countries have adopted food fortification strategies to combat iron deficiency, their effectiveness remains constrained, and high prevalence rates persist in many areas [25]. Globally, iron deficiency is closely linked to malnutrition, poverty, and poor sanitation, among other socioeconomic factors.

The disease burden caused by iron deficiency exhibits marked disparities across various regions, with areas of low SDI enduring the most of the burden According to the GBD 2021, iron deficiency has a profound impact on the physical activity, quality of life, and overall health status of affected individuals. Despite concerted global efforts to mitigate the burden of iron deficiency, the reduction in this burden is not consistent across different regions and genders [26]. For example, while East Asia and the Pacific, as well as South Asia, have achieved notable progress in controlling iron deficiency over the past several decades, men in Sub-Saharan Africa continue to grapple with a considerable burden [27]. In low SDI countries, the burden of nutritional deficiencies is particularly acute, especially among children, with the highest prevalence rates of iron deficiency and overall nutritional deficiencies reported in children aged 1–4 years [28]. Research indicates that from 1990 to 2019, there was a significant decline in the ASR incidence of iron deficiency and DALYs in low SDI countries [29]. However, in certain regions, such as Sub-Saharan Africa, the burden of iron deficiency persists at high levels [30]. This suggests that despite advancements made at the global level, there is a pressing need to redirect attention and resources to low SDI countries to support populations that are heavily burdened by iron deficiency, particularly women and men from lower socioeconomic backgrounds [31]. Moreover, iron deficiency is closely linked to the development of various chronic diseases, which further amplifies the health burden [24]. In some high-income countries, although overall health status has improved, the burden of iron deficiency and its associated diseases remains substantial, particularly among the elderly and those with chronic illnesses [32–34]. Therefore, strategies for the prevention and treatment of iron deficiency must be customized to the specific conditions of different regions to effectively alleviate its health impact.

Iron deficiency affects maternal health and fetal and neonatal development, potentially resulting in cognitive impairments and stunted growth. In Africa, the link between iron deficiency and infectious diseases, particularly malaria, is significant, as their synergistic effects exacerbate the health burden on children [35–37]. Various factors, including breast disorders, chronic illnesses, and malnutrition, can contribute to iron deficiency, which subsequently impacts maternal health [38]. Studies have shown that iron deficiency during pregnancy is strongly linked to a heightened risk of maternal and perinatal complications, such as premature birth and low birth weight [39–41]. Therefore, interventions aimed at addressing iron deficiency, such as the supplementation of iron and the promotion of dietary diversity, are crucial in mitigating these health risks [42]. The impact of iron deficiency on maternal and child health highlights the need for comprehensive strategies that prevent, and treat iron deficiency, and address its underlying socioeconomic and environmental factors [43]. These strategies must be culturally appropriate and tailored to the specific health needs of diverse populations to ensure that interventions reach those most in need.

Study limitations include the oversimplification of local contexts in the GBD 2021 data, exclusion of concurrent health interventions, temporal autocorrelation in the 1990–2021 time-series data, and complex interactions between iron deficiency and other health conditions. Future research should integrate local data, assess health interventions, and examine socio-economic factors contributing to iron deficiency persistence.

5. Conclusions

Overall, iron deficiency remains a major global health burden, with DALYs and deaths increasing from 1990 to 2021. Although ASRs have declined, absolute DALYs and deaths due to iron deficiency have risen, thereby highlighting the impact of population growth and aging on disease burden. Significant regional disparities exist, with low SDI areas experiencing the highest burden, particularly from maternal health disorders and dietary iron deficiency. Decomposition analysis reveals that population growth and epidemiological changes are key drivers of shifts in the disease due to iron deficiency. Notably, health disparities caused by iron deficiency have declined over time, albeit significant disparities persist in low-SDI regions. These findings highlight the need for targeted public health strategies to mitigate iron deficiency's impact on global health. Policymakers should prioritize interventions in low SDI regions by focusing on maternal health and dietary iron supplementation.

Abbreviations

GBD 2021, Global Burden of Disease Study 2021; HIV, Human Immunodeficiency Virus; DALYs, Disability-Adjusted Life Years; SDI, Socio-Demographic Index; BAPC, Bayesian age-period-cohort; EAPC, annual percentage change; ASR, age-standardized rates; UI, uncertainty interval; CI, confidence interval; AAPC, average annual percentage change; APC, annual percentage change.

Availability of Data and Materials

All datasets used in this study are publicly available and can be accessed at https://vizhub.healthdata.org/gbd-results/.

Author Contributions

SH and CG were instrumental in the conception and design of the study. SH and HL were primarily responsible for material preparation and data collection. HL, LZ and HC conducted the data analyses. SH and HL were involved in preparing the first draft of the manuscript, and all authors provided feedback and input on subsequent versions of the manuscript. All authors have read and approved the final version of the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR31351.

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