

Global, Regional, and National Epidemiology of Thalassemia in Childhood from 1990 to 2021

Yongle Li¹, Wanshuo Wei^{1,2}, Yuan Gan^{1,2}, Xiaomei Xie^{1,2}, Pengtao Qin^{1,2}, Liangsen Teng^{1,2}, Lihe Jiang^{1,3*}

¹School of Basic Medical Sciences, Youjiang Medical University for Nationalities, Baise, China

²School of Clinical Medicine, Youjiang Medical University for Nationalities, Baise, China

³Key Laboratory of Pollution Exposure and Health Intervention of Zhejiang Province, Interdisciplinary Research Academy, Zhejiang Shuren University, Hangzhou, China

Email: *jianglihe@ymun.edu.cn

How to cite this paper: Li, Y.L., Wei, W.S., Gan, Y., Xie, X.M., Qin, P.T., Teng, L.S. and Jiang, L.H. (2024) Global, Regional, and National Epidemiology of Thalassemia in Childhood from 1990 to 2021. *Journal of Biosciences and Medicines*, 12, 361-379.
<https://doi.org/10.4236/jbm.2024.1212029>

Received: November 14, 2024

Accepted: December 17, 2024

Published: December 20, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Objective: To analyze trends in prevalence, mortality, and disability-adjusted life years (DALYs) of childhood thalassemia from 1990 to 2021. **Methods:** Using the 2021 Global Burden of Disease (GBD) database, we conducted a cross-sectional study of children aged 0 - 14 years across 204 countries. We analyzed prevalence, mortality, and DALYs by region, country, age, sex, and Sociodemographic Index (SDI), calculating average annual percentage changes (EAPCs) to assess trends. **Results:** In 2021, there were 869,327 cases of childhood thalassemia globally. From 1990 to 2021, global prevalence decreased by 19.09%, and deaths declined from 12,018 to 5897. The mortality rate dropped from 0.69 to 0.29 per 100,000. High SDI regions had the lowest prevalence, mortality, and DALYs, all showing downward trends. Middle SDI regions had higher prevalence rates, while low and lower-middle SDI regions saw increases. Cambodia had the highest prevalence rate in 2021 (418 per 100,000), China had the highest number of cases (327,889), Pakistan had the highest DALYs (116987.40), and Guinea-Bissau had the highest DALYs rate (155.55 per 100,000). **Conclusions:** Childhood thalassemia remains a significant global health challenge. Despite declines in global prevalence, mortality, and DALYs, the burden remains high, especially in low SDI regions. Understanding the epidemiology of childhood thalassemia can aid in its prevention and control.

Keywords

Thalassemia, Childhood, Cross-Sectional Study

1. Introduction

Thalassemia is a group of inherited blood disorders that primarily affect the production of hemoglobin [1] [2], leading to chronic anemia and other serious health issues. This condition not only causes patients to feel fatigued and weak but can also trigger a range of other severe health problems, such as heart disease, liver complications, and skeletal deformities [3]-[6]. Although the global burden of thalassemia has been somewhat alleviated, it remains a significant public health challenge in many regions. Pediatric thalassemia not only impacts the quality of life of patients but also imposes a heavy economic burden on families and society.

Early research focused mainly on the genetic basis and clinical manifestations of thalassemia. Studies found that thalassemia is caused by mutations in the hemoglobin genes, leading to insufficient or structurally abnormal hemoglobin production. With the advancement of molecular biology techniques, scientists have gained deeper insights into the mechanisms of these genetic mutations, thereby promoting progress in the diagnosis and treatment of thalassemia.

Additionally, significant advancements have been made in the research on treatments for thalassemia. Traditional treatment methods primarily include regular blood transfusions and iron chelation therapy to alleviate anemia and prevent complications caused by iron overload. In recent years, emerging technologies such as gene therapy and stem cell transplantation have offered hope for a cure for thalassemia. However, the high costs and complexity of these new technologies present challenges to their widespread adoption and application.

The Global Burden of Disease (GBD) study provides a comprehensive database for assessing the disease burden across different regions and countries [7]. By analyzing data from the GBD database, we can better understand the epidemiological characteristics of thalassemia at global, regional, and national levels. This is crucial for formulating effective public health policies and resource allocation strategies.

This study aims to analyze the trends in prevalence, mortality, and disability-adjusted life years (DALYs) of pediatric thalassemia from 1990 to 2021. By conducting a stratified analysis of data across different regions, countries, ages, genders, and SDI areas, we hope to uncover the epidemiological dynamics of thalassemia and provide scientific evidence for future prevention and control measures.

2. Methods

2.1 Overview and Data Collection

Using the Global Health Data Exchange query tool created by GBD collaborators, we collected available data, standardized disease definitions, and prevalence information for children aged 0 to 14 years with thalassemia. The 2021 GBD study assessed the incidence, mortality, and DALYs of 371 diseases and injuries across 204 countries and regions from 1990 to 2021, with corresponding rates and uncertainty intervals, an increase from 369 in the 2019 edition. To summarize the age distribution of the burden of pediatric thalassemia, we

categorized patients into three groups: under 5 years, 5 to 9 years, and 10 to 14 years. In this study, we collected data on the number of thalassemia cases and prevalence, thalassemia-related mortality, and the number of disability-adjusted life years related to pediatric thalassemia, along with their corresponding rates at global, regional, and national levels. Data on the race and ethnicity of participants were not listed in the GBD database, which does not allocate data collection by race and ethnicity.

2.2. Sociodemographic Index

The Socio-demographic Index (SDI) is a measure of the development level of a country or region, based on data such as fertility rates, education levels, and per capita income [8]. The SDI ranges from 0 to 1, with higher levels indicating greater socio-economic development. It has been reported that SDI is associated with disease prevalence and mortality. This study categorizes countries and geographic regions into five SDI areas (low, lower-middle, middle, upper-middle, and high) to explore the relationship between the burden of pediatric thalassemia and socio-economic development.

2.3. Statistical Analysis

Incidence, mortality, DALYs, and their corresponding rates are the main indicators describing the burden of pediatric diabetes. These rates are reported per 100,000 people [9]. All calculations were performed using R4.4.1. By calculating the Estimated Annual Percentage Change (EAPCs), the dynamics of pediatric diabetes were analyzed to determine the time trends of the disease burden. This is of great significance for the formulation of public health policies and resource allocation.

3. Results

3.1. Global Trends in Childhood Thalassemia

Prevalence: In 2021, there were 869327.39 (708407.06 to 1065116.80) cases of thalassemia in children worldwide. Between 1990 and 2021, the global number of cases decreased by 6.41% (−5.37% to 7.22%). The corresponding prevalence decreased from 53.41 (44.59 to 64.11) in 1990 to 43.21 (35.21 to 52.94) in 2021. The prevalence of all children decreased with age (**Figure 1**).

Deaths: In 2021, the global number of thalassemia-related deaths in children was 5897.44 (3884.59, 7892.94), compared to 12017.59 (8270.41, 16293.83) in 1990, a decrease of 50.92% (−76.15%, −4.56%). The highest number of deaths in 1990 and 2021 were among children under 5 years of age, 9226.19 (5721.01 to 13107.82) and 4236.48 (2868.08 to 5928.82) respectively (**Figure 1**).

Disability-Adjusted Life Years (DALYs): Between 1990 and 2021, the number of thalassaemia-related disability-adjusted life years (DALYs) in children declined globally by about 50.08% (−74.60%, −4.29%). For both boys and girls, the older the age, the lower the incidence of DALYS (**Figure 1**).

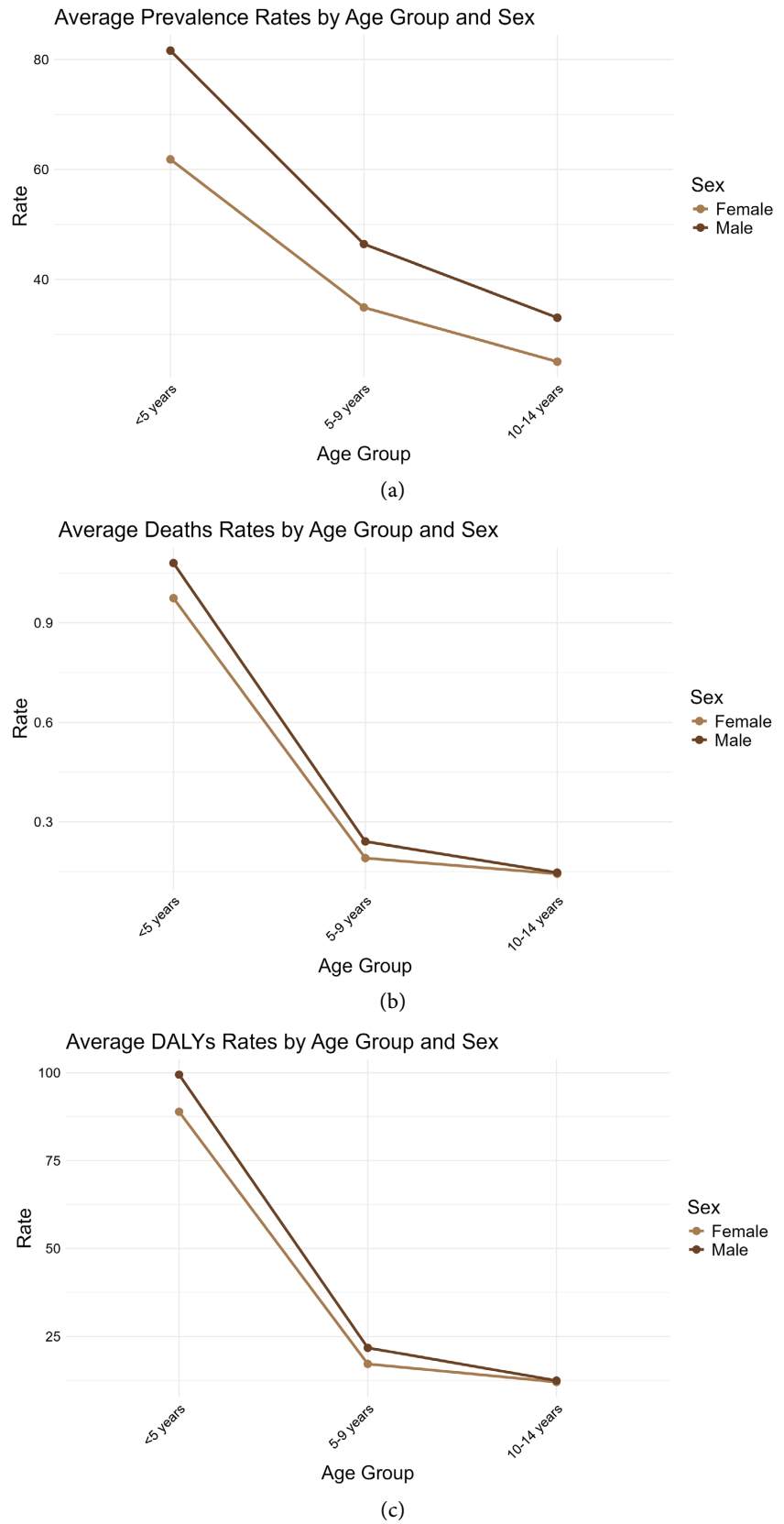


Figure 1. Trends in prevalence, mortality, and disability-adjusted life rate (DALYs) among children by age and sex.

3.2. Trends in SDI Regions for Pediatric Thalassemia

Prevalence: In 2021, the region with moderate SDI will have the highest number of cases of thalassemia in children, 388827.55 (314835.60 to 477709.51). The prevalence of High-middle SDI increased the most, to 463.67% (370.94 to 556.40). The prevalence of Middle SDI decreased the most, to -24.92% (-31.25 to 18.59). The largest decline was in the medium SDI region, with an EAPC of -0.86 (-1.17 to -0.56) (Table 1).

Table 1. Prevalence of thalassemia in children at global and regional levels, 1990-2021.

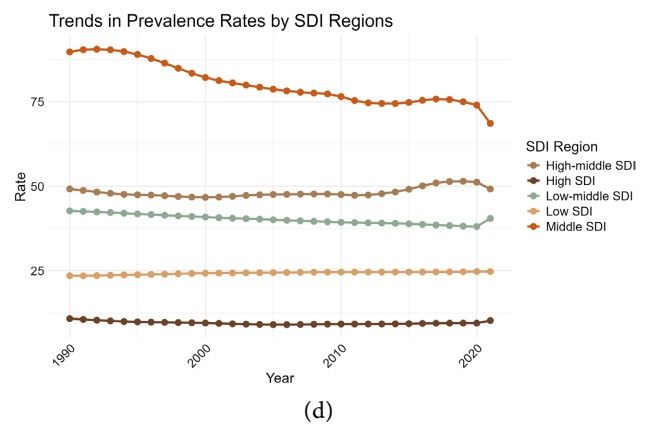
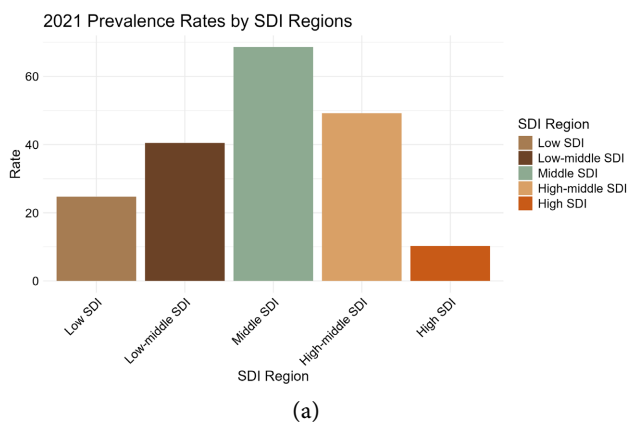
location_name	1990		2021		1990-2021	
	Prevalence number	Prevalence rate	Prevalence number	Prevalence rate	number change	EAPC
Global	928874.73 (775519.52 to 1115004.79)	53.41 (44.59 to 64.11)	869327.39 (708407.06 to 1065116.80)	43.21 (35.21 to 52.94)	-6.41% (-8.17 to -4.65)	-0.68% (-0.92 to -0.44)
High-middle SDI	20140.52 (108818.94 to 167381.63)	49.20 (39.77 to 61.17)	113563.87 (91269.60 to 139980.37)	49.19 (39.53 to 60.63)	463.67% (370.94 to 556.40)	0.00% (0.00 to 0.00)
High SDI	20140.52 (16361.35 to 24144.83)	10.84 (8.81 to 12.99)	17695.77 (14588.18 to 21300.00)	10.25 (8.46 to 12.35)	-12.12% (-15.42 to -8.82)	-0.18% (-0.24 to -0.12)
Low-middle SDI	201655.35 (171767.32 to 239310.81)	42.71 (36.38 to 50.69)	234702.62 (186206.80 to 300237.05)	40.48 (32.11 to 51.78)	16.38% (13.29 to 19.47)	-0.17% (-0.23 to -0.11)
Low SDI	53858.82 (43132.75 to 68150.26)	23.53 (18.84 to 29.77)	113951.82 (90646.69 to 146121.46)	24.76 (19.70 to 31.75)	111.52% (90.91 to 132.13)	0.16% (0.11 to 0.22)
Middle SDI	518055.36 (424965.42 to 625614.89)	89.75 (73.62 to 108.39)	388827.55 (314835.60 to 477709.52)	68.60 (55.54 to 84.27)	-24.92% (-31.25 to -18.59)	-0.86% (-1.17 to -0.56)
Southeast Asia	190359.50 (166548.21 to 220681.45)	111.49 (97.54 to 129.24)	177089.80 (143399.16 to 219882.52)	102.57 (83.06 to 127.35)	-6.97% (-8.88 to -5.06)	-0.27% (-0.36 to -0.17)
East Asia	456514.89 (353394.66 to 579115.05)	138.41 (107.14 to 175.58)	331293.01 (255461.11 to 423058.03)	123.92 (95.55 to 158.24)	-27.45% (-34.97 to -19.93)	-0.36% (-0.48 to -0.23)
Oceania	1276.58 (995.82 to 1603.62)	47.64 (37.16 to 59.84)	2585.18 (2008.21 to 3218.58)	50.88 (39.52 to 63.35)	102.48% (83.98 to 120.98)	0.21% (0.14 to 0.29)
Central Europe	4341.71 (3356.07 to 5457.51)	14.73 (11.38 to 18.51)	2638.82 (2018.72 to 3359.18)	14.91 (11.40 to 18.98)	-39.23% (-49.98 to -28.48)	0.04% (0.03 to 0.05)
Eastern Europe	9102.90 (6850.61 to 11908.01)	17.69 (13.31 to 23.14)	6424.33 (4858.40 to 8339.46)	18.13 (13.71 to 23.53)	-29.42% (-37.47 to -21.37)	0.08% (0.05 to 0.11)
Western Europe	8064.41 (6602.65 to 9523.50)	11.36 (9.30 to 13.41)	7195.03 (5936.52 to 8560.55)	10.56 (8.72 to 12.57)	-10.79% (-13.73 to -7.85)	-0.23% (-0.32 to -0.15)
Central Asia	5102.88 (4078.67 to 6311.21)	20.42 (16.32 to 25.25)	5674.85 (4513.41 to 7167.42)	20.50 (16.31 to 25.90)	11.21% (9.19 to 13.23)	0.01% (0.01 to 0.02)
Australasia	609.77 (462.22 to 785.51)	13.30 (10.08 to 17.13)	778.93 (583.91 to 1004.17)	13.59 (10.19 to 17.52)	27.74% (22.74 to 32.74)	0.07% (0.05 to 0.10)
Caribbean	2017.54 (1505.33 to 2599.75)	17.68 (13.19 to 22.78)	2390.71 (1793.70 to 3127.87)	20.78 (15.59 to 27.19)	18.51% (15.17 to 21.85)	0.52% (0.34 to 0.71)
Andean Latin America	2575.94 (1929.34 to 3429.03)	17.34 (12.99 to 23.09)	3518.80 (2600.92 to 4743.69)	19.45 (14.37 to 26.22)	36.61% (30.00 to 43.22)	0.37% (0.24 to 0.50)
High-income North America	2687.33 (2058.67 to 3464.33)	4.36 (3.34 to 5.62)	2014.03 (1692.45 to 2372.32)	3.07 (2.58 to 3.62)	-25.06% (-31.31 to -18.81)	-1.12% (-1.52 to -0.73)

Continued

High-income Asia Pacific	2814.38 (2255.24 to 3478.74)	8.00 (6.41 to 9.88)	1709.23 (1354.79 to 2131.59)	7.62 (6.04 to 9.51)	-39.27% (-49.99 to -28.55)	-0.15% (-0.21 to -0.10)
North Africa and Middle East	48583.99 (39771.09 to 58789.84)	34.58 (28.31 to 41.85)	60086.87 (47730.51 to 74729.12)	32.78 (26.04 to 40.76)	23.68% (19.39 to 27.97)	-0.17% (-0.23 to -0.11)
Southern Latin America	724.67 (569.13 to 923.52)	4.85 (3.81 to 6.19)	684.42 (526.32 to 863.13)	4.72 (3.63 to 5.95)	-5.56% (-7.08 to -4.04)	-0.09% (-0.12 to -0.06)
Tropical Latin America	8868.05 (6592.75 to 11553.21)	16.54 (12.30 to 21.55)	9774.18 (7289.84 to 12845.02)	19.47 (14.52 to 25.59)	10.20% (8.36 to 12.04)	0.53% (0.34 to 0.71)
Central Sub-Saharan Africa	5335.19 (3951.53 to 7209.70)	21.09 (15.62 to 28.50)	12565.46 (9195.91 to 16950.67)	21.41 (15.67 to 28.89)	135.51% (111.89 to 159.13)	0.05% (0.03 to 0.07)
Central Latin America	11744.93 (8735.45 to 15487.14)	18.24 (13.57 to 24.06)	13009.81 (9664.34 to 17083.80)	20.49 (15.22 to 26.91)	10.78% (8.83 to 12.73)	0.38% (0.24 to 0.51)
South Asia	119088.20 (101957.24 to 138808.71)	27.48 (23.53 to 32.03)	124230.98 (98494.68 to 158105.50)	24.50 (19.43 to 31.18)	4.32% (3.54 to 5.10)	-0.37% (-0.50 to -0.24)
Western Sub-Saharan Africa	21182.72 (16490.45 to 27184.96)	24.10 (18.76 to 30.93)	53050.43 (41321.14 to 68603.71)	24.70 (19.24 to 31.94)	150.45% (124.12 to 176.78)	0.08% (0.05 to 0.11)
Southern Sub-Saharan Africa	5162.17 (3963.81 to 6797.87)	24.95 (19.16 to 32.86)	6322.60 (4883.98 to 8309.34)	26.27 (20.29 to 34.53)	22.47% (18.54 to 26.40)	0.17% (0.11 to 0.23)
Eastern Sub-Saharan Africa	22716.99 (17780.24 to 29585.02)	25.08 (19.63 to 32.67)	46289.92 (36087.34 to 60079.53)	25.94 (20.22 to 33.67)	103.77% (85.00 to 122.54)	0.11% (0.07 to 0.15)

Deaths: Mortality rates decreased in all five SDI regions. The greatest reduction in mortality was seen in the medium-high SDI region, at 85.17% (85.11% to 85.24%). In 2021, the regions with the highest SDI had the lowest number of deaths, at 17695.77 (14588.18 to 21300.00). The number of deaths decreased with increasing SDI, and the mortality rate decreased with increasing SDI (Figure 2).

Disability-Adjusted Life Years (DALYs): In 2021, the number of DALYS will decrease with the increase of SDI, and the number of DALYS in low-SDI areas will be the highest, 220119.35 (146491.10 to 328060.66) (Figure 2).



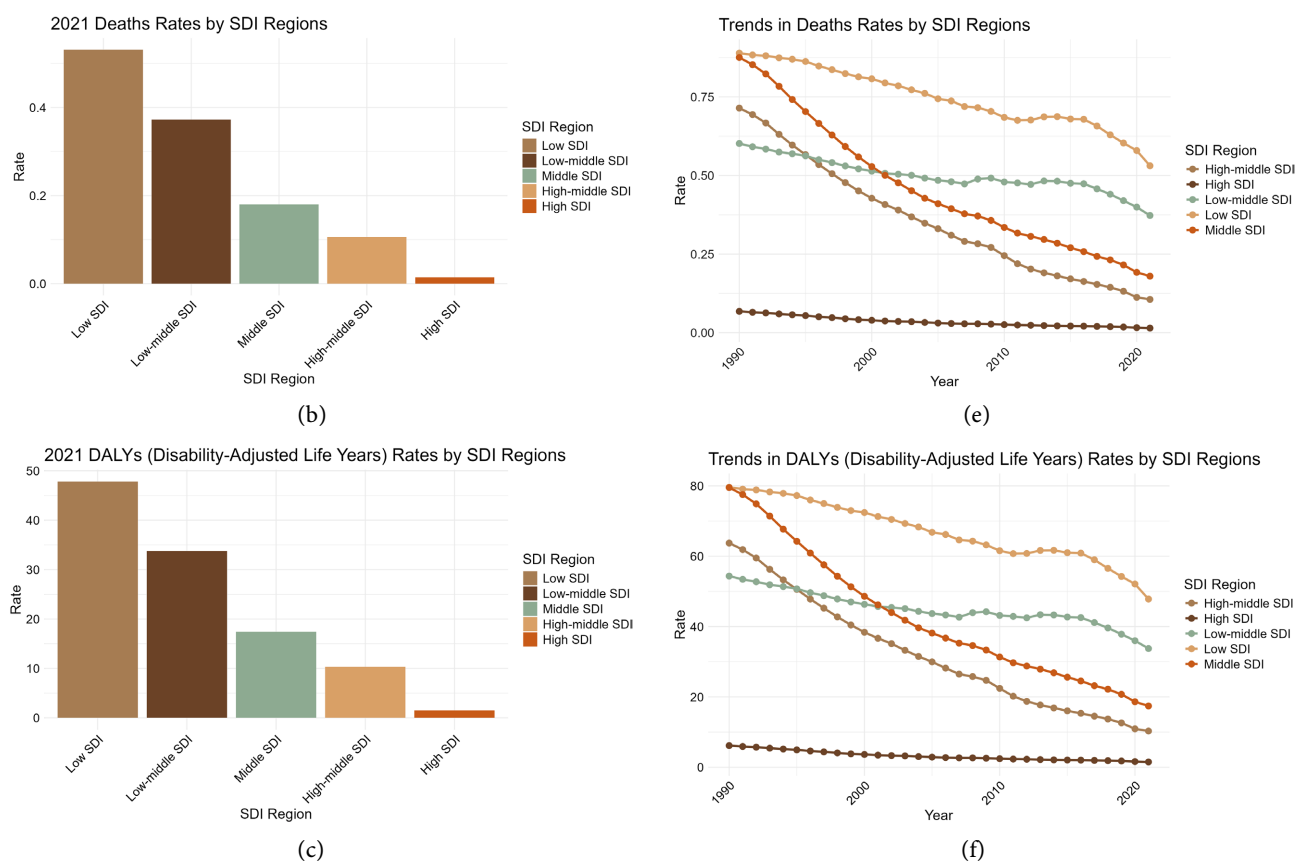


Figure 2. Prevalence, mortality, and disability-adjusted life rate (DALYs) in the five SDI regions in 2021.

3.3. Regional Trends in Pediatric Thalassemia

Prevalence: In 2021, East Asia will have the largest number of thalassemia cases in children with 331293.01 (255461.11 to 423058.03), followed by Southeast Asia and South Asia. The lowest number of cases was recorded in Southern Latin America, at 778.93 (583.91 to 1004.17). The highest prevalence was also found in East Asia, at 123.92 (95.55 to 158.24), followed by Southeast Asia, at 102.57 (83.05 to 127.35) (**Figure 3**). The largest downward trend in prevalence was in South Asia, with an EAPC of -0.37% (-0.50 to -0.24), and the largest upward trend was in Tropical Latin America, with an EAPC of 0.53% (0.34 to 0.71) (**Table 1**).

Deaths: West sub-Saharan Africa will have the highest number of deaths in 2021, at 1634.70 (982.98 to 2572.78). Western sub-Saharan Africa has the highest mortality rate of 0.76 (0.46 to 1.20) and high-income North America has the lowest mortality rate of 0.006 (0.004 to 0.006) (**Figure 3**). The largest decline in mortality was in East Asia, with an EAPC of -6.40 (-8.65 to -4.15) (**Table 1**).

Disability-Adjusted Life Years (DALYs): In 2021, children in western sub-Saharan Africa will have the highest number of thalassemia-related disability-adjusted life years (DALYs) of 147743.57 (89487.17 to 231580.15), while children in western sub-Saharan Africa will also have the highest DALYS rate. For 68.79 (41.67 to 107.83) (**Figure 3**). The decrease trend of DALYS rate was greatest in East Asia, with EAPC of -6.06 (-8.19 to -3.93) (**Table 1**).

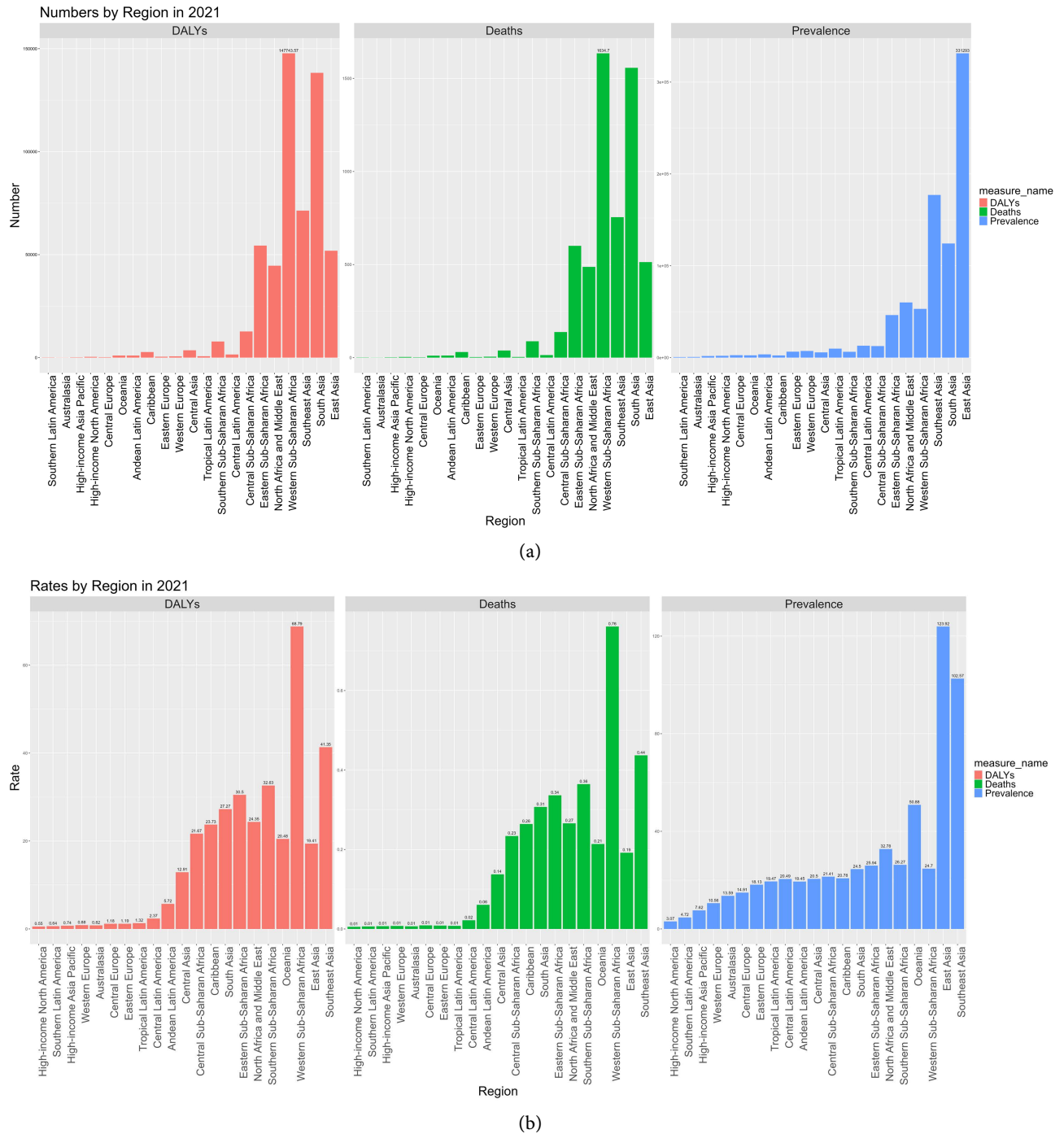


Figure 3. Comparison of prevalence, mortality rates, and disability-adjusted life year rates (DALYs) by region in 2021.

3.4. National Trends in Pediatric Thalassemia

Prevalence: The country with the highest prevalence of thalassemia in children in 2021 is Cambodia, at 418.00 (312.89 to 543.84). The country with the highest number of cases is China, with 327888.97 (252513.83 to 419321.84). Brazil had the largest increase in Mediterranean cases in children, with an EAPC of 0.54 (0.72 to 0.35) (Table 2). The largest decline was in the United States of America, with an

EAPC of -1.29 (-1.74 to -0.84) (**Table 2**).

Deaths: The highest number of thalassemia-related deaths in children in 2021 was in Pakistan, with 1360.96 (684.21 to 2175.62). The highest mortality rate was recorded in Guinea-Bissau, at 1.77 (0.36 to 9.34). The country with the largest increase in mortality was Tokelau, with an EAPC of 3.04 (1.97 to 4.11) (**Table 2**). The largest reduction in mortality was seen in Grenada, with an EAPC of -15.97 (-21.59 to -10.35) (**Table 2**).

Disability-Adjusted Life Years (DALYs): The highest number of DALYs in children with thalassemia in 2021 was in Pakistan, 116987.40 (59694.77 to 185535.93), and the highest DALYs rate was in Guinea-Bissau, 155.55 (32.67 to 816.01). Tokelau saw the largest increase in DALYs, with an EAPC of 2.76 (1.79 to 3.74) (**Table 2**), and Saudi Arabia saw the largest decrease in DALYs, with an EAPC of -6.53 (-8.83 to -4.23) (**Table 2**).

Table 2. Estimated annual percentage change (EAPC) of prevalence, deaths, and disability-adjusted life years (DALYs) in 204 countries from 1990 to 2021.

location_name	Prevalence			Deaths			Disability-Adjusted Life Years (DALYs)		
	EAPC	CI_lower	CI_upper	EAPC	CI_lower	CI_upper	EAPC	CI_lower	CI_upper
Afghanistan	0.170218	0.110297	0.23014	-2.55291	-1.65422	-3.4516	-2.52507	-1.63618	-3.41396
Albania	-0.51335	-0.33264	-0.69406	-4.27884	-2.77257	-5.7851	-4.17647	-2.70624	-5.6467
Algeria	0.031286	0.020272	0.042299	-4.08565	-2.64739	-5.52391	-3.98942	-2.58504	-5.39381
American Samoa	-0.26952	-0.17464	-0.3644	-0.87094	-0.56435	-1.17754	-0.92591	-0.59997	-1.25186
Andorra	-0.10572	-0.0685	-0.14293	-5.85894	-3.79644	-7.92144	-5.09504	-3.30145	-6.88862
Angola	0.089335	0.057887	0.120784	-3.47077	-2.24897	-4.69257	-3.3601	-2.17726	-4.54295
Antigua and Barbuda	0.344536	0.22325	0.465822	-6.31432	-4.09152	-8.53713	-2.75138	-1.78282	-3.71994
Argentina	-0.10323	-0.06689	-0.13957	-4.7893	-3.10334	-6.47526	-4.53667	-2.93964	-6.13369
Armenia	-0.11213	-0.07266	-0.1516	-3.16591	-2.05143	-4.28039	-2.80697	-1.81884	-3.79509
Australia	0.061217	0.039667	0.082767	-4.02898	-2.61067	-5.44728	-3.43595	-2.2264	-4.64549
Austria	-0.07389	-0.04788	-0.09991	-4.38459	-2.8411	-5.92808	-2.95896	-1.91733	-4.00059
Azerbaijan	-0.48156	-0.31204	-0.65108	-3.44045	-2.22932	-4.65158	-3.43945	-2.22867	-4.65023
Bahamas	0.330827	0.214367	0.447287	-5.68682	-3.68491	-7.68873	-0.57873	-0.375	-0.78246
Bahrain	-0.26867	-0.17409	-0.36324	-4.12362	-2.672	-5.57524	-4.04265	-2.61953	-5.46578
Bangladesh	0.036825	0.023862	0.049789	-4.0026	-2.59358	-5.41161	-3.55812	-2.30557	-4.81067
Barbados	0.370646	0.240169	0.501123	-5.45277	-3.53325	-7.37229	-2.98505	-1.93423	-4.03587
Belarus	0.161614	0.104722	0.218506	-0.29197	-0.18919	-0.39475	-0.5479	-0.35502	-0.74077
Belgium	-0.11968	-0.07755	-0.16181	-3.93662	-2.55083	-5.32242	-3.27254	-2.12052	-4.42456
Belize	0.305624	0.198036	0.413211	-2.80999	-1.8208	-3.79918	-1.96426	-1.27279	-2.65573

Continued

Benin	0.162752	0.105459	0.220045	-3.07721	-1.99395	-4.16047	-3.03781	-1.96842	-4.10719
Bermuda	0.359475	0.23293	0.48602	-0.69151	-0.44808	-0.93493	-0.46359	-0.30039	-0.62678
Bhutan	-0.15709	-0.10179	-0.21239	-3.02005	-1.95691	-4.08319	-2.87932	-1.86572	-3.89292
Bolivia (Plurinational State of)	0.270249	0.175114	0.365383	-4.07089	-2.63783	-5.50396	-3.96439	-2.56882	-5.35996
Bosnia and Herzegovina	-0.07009	-0.04542	-0.09477	-4.35461	-2.82167	-5.88754	-3.70594	-2.40135	-5.01053
Botswana	0.159813	0.103555	0.216072	-0.23516	-0.15238	-0.31795	-0.22931	-0.14859	-0.31003
Brazil	0.535117	0.346742	0.723492	-3.34395	-2.16679	-4.52111	-1.72355	-1.11682	-2.33029
Brunei Darussalam	-0.24114	-0.15625	-0.32602	-2.25985	-1.46432	-3.05537	-2.15081	-1.39367	-2.90795
Bulgaria	0.125999	0.081644	0.170354	-2.70934	-1.75558	-3.66309	-2.29153	-1.48485	-3.09821
Burkina Faso	0.203144	0.131632	0.274657	-1.80102	-1.16702	-2.43503	-1.76441	-1.14329	-2.38553
Burundi	0.183328	0.118792	0.247864	-2.81994	-1.82724	-3.81263	-2.77485	-1.79803	-3.75168
Cabo Verde	0.088426	0.057297	0.119554	-3.72457	-2.41342	-5.03572	-3.66231	-2.37308	-4.95153
Cambodia	0.244668	0.158538	0.330797	-3.03595	-1.96721	-4.10468	-2.55188	-1.65355	-3.45021
Cameroon	0.058857	0.038138	0.079577	-1.63004	-1.05623	-2.20386	-1.62161	-1.05076	-2.19246
Canada	-0.29016	-0.18802	-0.3923	-3.41945	-2.21571	-4.62318	-3.03546	-1.9669	-4.10403
Central African Republic	0.038935	0.025229	0.052642	-1.72244	-1.1161	-2.32879	-1.69786	-1.10017	-2.29556
Chad	0.162012	0.104979	0.219044	-1.12882	-0.73145	-1.5262	-1.12625	-0.72978	-1.52271
Chile	-0.09239	-0.05987	-0.12492	-4.57128	-2.96207	-6.18049	-3.63557	-2.35575	-4.91539
China	-0.37524	-0.24315	-0.50734	-6.49132	-4.2062	-8.77643	-6.14163	-3.97962	-8.30365
Colombia	0.382675	0.247964	0.517387	-2.15914	-1.39906	-2.91921	-1.19543	-0.77461	-1.61625
Comoros	0.260092	0.168533	0.351652	-1.93084	-1.25113	-2.61054	-1.92548	-1.24766	-2.60329
Congo	0.069769	0.045208	0.094329	-3.07016	-1.98938	-4.15093	-3.01212	-1.95178	-4.07247
Cook Islands	-0.14772	-0.09572	-0.19972	-3.07814	-1.99455	-4.16172	-2.73506	-1.77225	-3.69788
Costa Rica	0.355697	0.230482	0.480912	-3.68081	-2.38507	-4.97655	-1.78482	-1.15652	-2.41312
Croatia	0.196236	0.127156	0.265317	-2.88127	-1.86699	-3.89555	-1.28657	-0.83366	-1.73947
Cuba	0.326069	0.211284	0.440854	-6.36912	-4.12702	-8.61122	-2.41624	-1.56566	-3.26682
Cyprus	-0.46801	-0.30326	-0.63276	-5.31048	-3.44105	-7.17991	-4.60229	-2.98216	-6.22242
Czechia	0.291336	0.188778	0.393893	-2.92673	-1.89644	-3.95702	-1.18238	-0.76615	-1.59861
Côte d'Ivoire	0.021971	0.014237	0.029706	-1.83047	-1.1861	-2.47485	-1.79856	-1.16542	-2.4317
Democratic People's Republic of Korea	-0.17227	-0.11163	-0.23291	-3.05248	-1.97793	-4.12704	-2.99281	-1.93926	-4.04636
Democratic Republic of the Congo	0.040429	0.026197	0.054661	-2.51556	-1.63002	-3.40111	-2.47334	-1.60266	-3.34403

Continued

Denmark	0.000503	0.000326	0.000679	-3.45851	-2.24102	-4.67599	-2.56248	-1.66042	-3.46454
Djibouti	0.247051	0.160082	0.334019	-2.32935	-1.50936	-3.14935	-2.27817	-1.47619	-3.08014
Dominica	0.255508	0.165563	0.345454	0.282006	0.182732	0.381279	0.243374	0.1577	0.329048
Dominican Republic	0.383351	0.248401	0.5183	-2.50206	-1.62127	-3.38285	-2.41598	-1.56549	-3.26646
Ecuador	0.337007	0.218372	0.455643	-5.85323	-3.79274	-7.91372	-0.30902	-0.20024	-0.4178
Egypt	0.049325	0.031961	0.066688	-2.94725	-1.90974	-3.98476	-2.84916	-1.84618	-3.85214
El Salvador	0.407579	0.264101	0.551058	-3.95048	-2.5598	-5.34115	-3.89837	-2.52604	-5.27069
Equatorial Guinea	-0.10676	-0.06918	-0.14434	-3.98247	-2.58054	-5.38441	-3.73219	-2.41836	-5.04602
Eritrea	0.242748	0.157294	0.328201	-1.19277	-0.77289	-1.61266	-1.17089	-0.7587	-1.58307
Estonia	0.130941	0.084846	0.177035	-3.63243	-2.35372	-4.91114	-1.05044	-0.68066	-1.42022
Eswatini	0.13911	0.090139	0.18808	-0.71634	-0.46417	-0.9685	-0.70981	-0.45994	-0.95968
Ethiopia	0.156291	0.101273	0.211131	-3.27518	-2.12223	-4.42813	-3.21296	-2.08191	-4.344
Fiji	-0.03636	-0.02356	-0.04915	-0.14878	-0.0964	-0.20115	-0.15912	-0.1031	-0.21513
Finland	-0.11288	-0.07315	-0.15262	-2.64416	-1.71334	-3.57497	-1.42202	-0.92143	-1.9226
France	-0.13961	-0.09047	-0.18876	-3.79923	-2.4618	-5.13666	-3.00974	-1.95023	-4.06925
Gabon	0.039713	0.025733	0.053693	-2.21053	-1.43237	-2.9887	-2.15485	-1.39628	-2.91341
Gambia	0.11011	0.071348	0.148872	-2.04251	-1.32349	-2.76153	-2.02418	-1.31161	-2.73674
Georgia	0.458016	0.296782	0.619249	-0.12358	-0.08008	-0.16708	-0.05934	-0.03845	-0.08022
Germany	0.285636	0.185084	0.386187	-3.13866	-2.03377	-4.24355	-2.71519	-1.75937	-3.67101
Ghana	0.112561	0.072937	0.152186	-2.43627	-1.57864	-3.2939	-2.41455	-1.56457	-3.26454
Greece	-0.19738	-0.1279	-0.26686	-4.64633	-3.0107	-6.28197	-4.18552	-2.71211	-5.65893
Greenland	-0.00625	-0.00405	-0.00845	-2.51848	-1.63191	-3.40505	-2.2523	-1.45943	-3.04517
Grenada	0.298026	0.193113	0.402939	-15.9666	-10.346	-21.5873	-5.4256	-3.51565	-7.33556
Guam	-0.11995	-0.07772	-0.16217	-4.45737	-2.88826	-6.02649	-3.19685	-2.07148	-4.32223
Guatemala	0.280187	0.181554	0.37882	-2.86716	-1.85785	-3.87648	-1.20982	-0.78393	-1.63571
Guinea	0.039306	0.025469	0.053143	-2.13575	-1.38391	-2.88759	-2.1127	-1.36897	-2.85643
Guinea-Bissau	0.244126	0.158187	0.330065	-2.96593	-1.92184	-4.01001	-2.96386	-1.9205	-4.00722
Guyana	0.18539	0.120128	0.250652	-7.20253	-4.66705	-9.73801	-5.52435	-3.57964	-7.46907
Haiti	0.35156	0.227802	0.475319	-1.35936	-0.88083	-1.83788	-1.34337	-0.87047	-1.81627
Honduras	0.462596	0.29975	0.625441	-4.20443	-2.72436	-5.6845	-4.15599	-2.69297	-5.61901
Hungary	0.263448	0.170708	0.356189	-2.47497	-1.60372	-3.34623	-1.316	-0.85273	-1.77926
Iceland	-0.06933	-0.04493	-0.09374	-2.63397	-1.70675	-3.5612	-0.56753	-0.36775	-0.76732
India	-0.25221	-0.16342	-0.34099	-3.74366	-2.42579	-5.06153	-3.41545	-2.21312	-4.61777
Indonesia	0.356334	0.230895	0.481773	-2.40675	-1.55951	-3.254	-2.35198	-1.52402	-3.17994

Continued

Iran (Islamic Republic of)	-0.16318	-0.10574	-0.22063	-6.08388	-3.94219	-8.22557	-5.87132	-3.80446	-7.93818
Iraq	-0.19895	-0.12892	-0.26899	-4.25355	-2.75619	-5.75091	-4.08231	-2.64523	-5.51939
Ireland	-0.0355	-0.023	-0.04799	-4.7873	-3.10205	-6.47256	-2.98131	-1.93181	-4.0308
Israel	-0.18687	-0.12108	-0.25265	-4.9029	-3.17695	-6.62885	-4.53006	-2.93536	-6.12476
Italy	0.099508	0.064478	0.134537	-5.02816	-3.25811	-6.7982	-4.25203	-2.7552	-5.74886
Jamaica	0.344643	0.22332	0.465967	-4.88671	-3.16646	-6.60695	-0.82323	-0.53343	-1.11303
Japan	-0.07542	-0.04887	-0.10196	-5.58619	-3.61971	-7.55268	-4.55898	-2.9541	-6.16387
Jordan	-0.37765	-0.24471	-0.51059	-3.72181	-2.41163	-5.03198	-3.60248	-2.33431	-4.87064
Kazakhstan	0.21118	0.136839	0.285521	1.675702	1.08581	2.265593	0.880589	0.570598	1.190579
Kenya	0.015631	0.010129	0.021134	-1.45025	-0.93973	-1.96078	-1.38057	-0.89457	-1.86656
Kiribati	-0.18651	-0.12085	-0.25216	-2.13484	-1.38332	-2.88636	-2.14768	-1.39164	-2.90372
Kuwait	0.122793	0.079567	0.166019	-1.53316	-0.99344	-2.07287	-1.40504	-0.91043	-1.89966
Kyrgyzstan	0.062663	0.040604	0.084722	-1.73343	-1.12322	-2.34364	-1.25914	-0.81589	-1.7024
Lao People's Democratic Republic	0.368667	0.238887	0.498448	-2.86792	-1.85833	-3.8775	-2.50646	-1.62412	-3.3888
Latvia	0.133543	0.086532	0.180553	-3.81046	-2.46908	-5.15184	-0.94058	-0.60947	-1.27169
Lebanon	-0.31344	-0.2031	-0.42378	-4.076	-2.64114	-5.51085	-3.8712	-2.50844	-5.23396
Lesotho	0.076365	0.049483	0.103248	0.24538	0.159	0.33176	0.202346	0.131115	0.273577
Liberia	-0.12625	-0.08181	-0.1707	-3.62826	-2.35102	-4.9055	-3.58231	-2.32124	-4.84338
Libya	-0.23095	-0.14965	-0.31224	-2.8158	-1.82457	-3.80704	-2.5745	-1.66821	-3.48079
Lithuania	0.154333	0.100004	0.208663	-2.54075	-1.64634	-3.43516	-0.99802	-0.64669	-1.34935
Luxembourg	0.026007	0.016852	0.035163	-5.67825	-3.67936	-7.67715	-3.94855	-2.55856	-5.33854
Madagascar	0.05389	0.034919	0.072861	-2.4182	-1.56693	-3.26947	-2.37262	-1.5374	-3.20785
Malawi	-0.02782	-0.01803	-0.03762	-3.61149	-2.34015	-4.88283	-3.57779	-2.31831	-4.83727
Malaysia	-0.24434	-0.15833	-0.33035	-3.7788	-2.44856	-5.10904	-3.48574	-2.25867	-4.71282
Maldives	-0.38681	-0.25064	-0.52298	-4.41996	-2.86402	-5.97591	-4.00258	-2.59357	-5.4116
Mali	0.11595	0.075133	0.156768	-2.46085	-1.59457	-3.32714	-2.43373	-1.57699	-3.29047
Malta	0.258578	0.167552	0.349604	-1.36291	-0.88313	-1.84269	-1.34154	-0.86928	-1.8138
Marshall Islands	-0.10118	-0.06556	-0.13679	-1.11272	-0.72101	-1.50443	-1.04566	-0.67756	-1.41377
Mauritania	0.063963	0.041446	0.086479	-2.73198	-1.77025	-3.69371	-2.69669	-1.74739	-3.646
Mauritius	0.083588	0.054163	0.113013	-0.8354	-0.54131	-1.12948	-0.7504	-0.48624	-1.01457
Mexico	0.353346	0.228959	0.477733	-1.95493	-1.26674	-2.64311	-0.96373	-0.62447	-1.30299
Micronesia (Federated States of)	-0.11412	-0.07395	-0.15429	-3.07444	-1.99216	-4.15672	-2.7936	-1.81018	-3.77702

Continued

Monaco	-0.15681	-0.10161	-0.21201	-3.06168	-1.98388	-4.13947	-2.71358	-1.75833	-3.66883
Mongolia	0.221198	0.143331	0.299066	-3.75487	-2.43306	-5.07668	-3.66229	-2.37307	-4.95151
Montenegro	0.196391	0.127256	0.265526	-3.90018	-2.52722	-5.27315	-3.32877	-2.15696	-4.50059
Morocco	-0.1356	-0.08786	-0.18333	-4.24457	-2.75037	-5.73877	-4.15213	-2.69047	-5.61379
Mozambique	0.269815	0.174833	0.364797	-2.64133	-1.71151	-3.57115	-2.6107	-1.69166	-3.52973
Myanmar	0.451772	0.292736	0.610808	-2.59999	-1.68473	-3.51526	-2.36328	-1.53134	-3.19522
Namibia	0.148105	0.095968	0.200242	-0.82498	-0.53457	-1.1154	-0.81994	-0.5313	-1.10857
Nauru	-0.1269	-0.08223	-0.17157	-1.50752	-0.97683	-2.0382	-1.42567	-0.9238	-1.92754
Nepal	-0.05534	-0.03586	-0.07482	-4.47118	-2.89721	-6.04516	-4.28733	-2.77807	-5.79658
Netherlands	-0.02075	-0.01345	-0.02805	-4.64474	-3.00967	-6.27981	-3.96624	-2.57002	-5.36246
New Zealand	0.117875	0.07638	0.15937	-5.22238	-3.38396	-7.06079	-3.52951	-2.28703	-4.77199
Nicaragua	0.401501	0.260162	0.54284	-4.87199	-3.15692	-6.58705	-4.79715	-3.10843	-6.48588
Niger	0.159297	0.10322	0.215374	-3.48219	-2.25637	-4.70802	-3.39825	-2.20198	-4.59453
Nigeria	0.120131	0.077841	0.16242	-0.96904	-0.62792	-1.31017	-0.9601	-0.62212	-1.29808
Niue	-0.1519	-0.09843	-0.20537	2.680798	1.737087	3.62451	2.430342	1.574797	3.285887
North Macedonia	0.054668	0.035424	0.073913	-6.06841	-3.93217	-8.20465	-5.5231	-3.57882	-7.46738
Northern Mariana Islands	-0.19437	-0.12595	-0.26279	-4.14285	-2.68446	-5.60125	-2.86039	-1.85346	-3.86732
Norway	-0.17824	-0.11549	-0.24098	-6.21472	-4.02697	-8.40246	-2.79766	-1.81281	-3.78251
Oman	-0.11004	-0.0713	-0.14878	-4.15492	-2.69228	-5.61756	-3.97191	-2.57369	-5.37013
Pakistan	-0.71218	-0.46148	-0.96289	-0.83077	-0.53832	-1.12322	-0.85213	-0.55216	-1.15211
Palau	-0.13323	-0.08633	-0.18013	-2.93337	-1.90075	-3.966	-2.60676	-1.68911	-3.52441
Palestine	-0.2321	-0.15039	-0.3138	-3.90237	-2.52863	-5.27611	-3.78636	-2.45346	-5.11925
Panama	0.423043	0.274121	0.571966	-2.11983	-1.3736	-2.86607	-1.52202	-0.98623	-2.05781
Papua New Guinea	0.113215	0.07336	0.153069	-1.20233	-0.77908	-1.62559	-1.10972	-0.71907	-1.50037
Paraguay	0.358985	0.232613	0.485357	-1.51917	-0.98438	-2.05395	-1.48263	-0.96071	-2.00456
Peru	0.410729	0.266142	0.555317	-4.66966	-3.02582	-6.3135	-4.49158	-2.91043	-6.07274
Philippines	0.062479	0.040485	0.084473	-2.59659	-1.68252	-3.51066	-2.5658	-1.66257	-3.46903
Poland	-0.06242	-0.04044	-0.08439	-6.38559	-4.1377	-8.63349	-2.51257	-1.62808	-3.39705
Portugal	-0.10047	-0.0651	-0.13584	-5.7661	-3.73628	-7.79592	-5.07526	-3.28863	-6.86188
Puerto Rico	0.344741	0.223383	0.466099	-6.33121	-4.10245	-8.55996	-0.45034	-0.29181	-0.60887
Qatar	-0.1634	-0.10588	-0.22093	-5.19144	-3.36392	-7.01896	-4.62996	-3.00009	-6.25983
Republic of Korea	-0.13587	-0.08804	-0.18371	-6.38072	-4.13454	-8.62691	-5.93062	-3.84289	-8.01836
Republic of Moldova	0.098613	0.063899	0.133328	-1.96621	-1.27405	-2.65836	-1.55547	-1.00791	-2.10304

Continued

Romania	0.209643	0.135843	0.283443	-4.60025	-2.98084	-6.21965	-3.48517	-2.2583	-4.71205
Russian Federation	0.068319	0.044269	0.09237	-2.08746	-1.35262	-2.8223	-1.50768	-0.97694	-2.03842
Rwanda	0.199902	0.129531	0.270272	-3.13351	-2.03043	-4.23658	-3.09365	-2.0046	-4.18269
Saint Kitts and Nevis	0.381153	0.246977	0.515329	-1.55503	-1.00762	-2.10244	-0.82187	-0.53255	-1.1112
Saint Lucia	0.35708	0.231379	0.482782	0.822003	0.532636	1.11137	-0.21515	-0.13941	-0.29089
Saint Vincent and the Grenadines	0.396145	0.256692	0.535599	-5.30559	-3.43788	-7.17329	-1.387	-0.89874	-1.87526
Samoa	-0.03592	-0.02327	-0.04856	-2.68799	-1.74175	-3.63424	-2.40809	-1.56038	-3.25581
San Marino	0.203516	0.131873	0.275159	-5.17	-3.35002	-6.98997	-4.02948	-2.611	-5.44796
Sao Tome and Principe	0.096626	0.062611	0.130641	-4.4681	-2.89521	-6.04099	-4.36644	-2.82934	-5.90355
Saudi Arabia	-0.13337	-0.08642	-0.18032	-6.92187	-4.48519	-9.35855	-6.53282	-4.23309	-8.83254
Senegal	0.118371	0.076701	0.160041	-2.67114	-1.73083	-3.61145	-2.63775	-1.7092	-3.56631
Serbia	0.091993	0.059609	0.124378	-6.45049	-4.17975	-8.72124	-5.67919	-3.67997	-7.67842
Seychelles	-0.01591	-0.01031	-0.0215	-2.8354	-1.83726	-3.83354	-2.59127	-1.67908	-3.50347
Sierra Leone	0.015863	0.010279	0.021447	-2.06853	-1.34035	-2.79671	-2.03977	-1.32172	-2.75782
Singapore	-0.3149	-0.20405	-0.42576	-6.79255	-4.40139	-9.1837	-6.26825	-4.06166	-8.47484
Slovakia	0.134213	0.086966	0.181459	-3.65713	-2.36972	-4.94453	-3.03051	-1.96369	-4.09733
Slovenia	0.211908	0.137311	0.286505	-3.23689	-2.09742	-4.37636	-1.19727	-0.7758	-1.61874
Solomon Islands	-0.11087	-0.07184	-0.1499	-2.06569	-1.33851	-2.79286	-1.88798	-1.22336	-2.5526
Somalia	0.375828	0.243526	0.508129	-1.55438	-1.0072	-2.10157	-1.51961	-0.98467	-2.05456
South Africa	0.134444	0.087116	0.181772	-1.37917	-0.89367	-1.86468	-1.32342	-0.85754	-1.7893
South Sudan	0.14857	0.096269	0.200871	-0.72489	-0.46971	-0.98007	-0.74011	-0.47957	-1.00065
Spain	0.079167	0.051298	0.107036	-3.91345	-2.53581	-5.29109	-3.40917	-2.20905	-4.60929
Sri Lanka	0.139718	0.090533	0.188902	-5.16692	-3.34803	-6.98581	-4.86851	-3.15466	-6.58235
Sudan	-0.12625	-0.08181	-0.17069	-4.11449	-2.66608	-5.5629	-4.03723	-2.61602	-5.45845
Suriname	0.398284	0.258077	0.53849	-1.77719	-1.15157	-2.40281	-1.71442	-1.1109	-2.31794
Sweden	-0.03025	-0.0196	-0.0409	-3.99796	-2.59057	-5.40534	-2.77601	-1.79878	-3.75324
Switzerland	0.007796	0.005052	0.010541	-3.86175	-2.50231	-5.22119	-3.25456	-2.10887	-4.40026
Syrian Arab Republic	-0.48379	-0.31348	-0.6541	-3.99448	-2.58832	-5.40064	-3.98334	-2.5811	-5.38558
Taiwan (Province of China)	0.506712	0.328336	0.685087	1.75767	1.138924	2.376416	1.566251	1.014889	2.117613
Tajikistan	-0.29219	-0.18933	-0.39505	-2.37294	-1.5376	-3.20828	-2.31801	-1.50201	-3.13401
Thailand	-0.1348	-0.08735	-0.18226	-6.54808	-4.24299	-8.85318	-5.11143	-3.31207	-6.91078
Timor-Leste	-0.13564	-0.08789	-0.18339	-2.82754	-1.83217	-3.82291	-2.77763	-1.79983	-3.75543
Togo	0.149509	0.096878	0.20214	-2.31728	-1.50154	-3.13302	-2.28878	-1.48307	-3.0945

Continued

Tokelau	-0.19051	-0.12344	-0.25757	3.040014	1.969849	4.110179	2.762699	1.790156	3.735242
Tonga	-0.04111	-0.02664	-0.05558	-1.9049	-1.23433	-2.57548	-1.67722	-1.0868	-2.26765
Trinidad and Tobago	0.278181	0.180254	0.376108	-3.46309	-2.24399	-4.68219	-3.05107	-1.97701	-4.12512
Tunisia	-0.32138	-0.20825	-0.43452	-4.9349	-3.19768	-6.67211	-4.72614	-3.06241	-6.38987
Turkey	0.010793	0.006994	0.014592	-5.63985	-3.65447	-7.62522	-5.515	-3.57357	-7.45642
Turkmenistan	0.113876	0.073789	0.153964	1.217122	0.788663	1.645581	0.900771	0.583676	1.217867
Tuvalu	-0.25877	-0.16768	-0.34987	-4.18363	-2.71088	-5.65638	-3.93227	-2.54801	-5.31653
Uganda	0.035603	0.02307	0.048136	-1.80192	-1.16759	-2.43624	-1.79574	-1.16359	-2.42789
Ukraine	-0.00764	-0.00495	-0.01033	-2.81711	-1.82542	-3.80881	-2.41827	-1.56698	-3.26957
United Arab Emirates	-0.50211	-0.32535	-0.67887	-5.24413	-3.39806	-7.09021	-4.81269	-3.11849	-6.50688
United Kingdom	-0.07014	-0.04545	-0.09483	-0.03996	-0.02589	-0.05402	-0.07336	-0.04754	-0.09919
United Republic of Tanzania	0.084599	0.054818	0.11438	-1.60547	-1.0403	-2.17064	-1.6095	-1.04291	-2.17608
United States of America	-1.28956	-0.8356	-1.74352	-3.82361	-2.4776	-5.16962	-3.63334	-2.35431	-4.91237
United States Virgin Islands	0.419905	0.272087	0.567722	-4.2334	-2.74313	-5.72367	-3.56291	-2.30867	-4.81715
Uruguay	-0.13219	-0.08566	-0.17873	-4.67974	-3.03235	-6.32713	-4.358	-2.82387	-5.89213
Uzbekistan	-0.02777	-0.01799	-0.03754	0.083683	0.054225	0.113142	-0.01858	-0.01204	-0.02512
Vanuatu	-0.11695	-0.07578	-0.15811	-1.79795	-1.16502	-2.43087	-1.60628	-1.04083	-2.17174
Venezuela (Bolivarian Republic of)	0.428484	0.277646	0.579322	-1.3434	-0.87049	-1.81631	-0.7677	-0.49745	-1.03795
Viet Nam	-0.14905	-0.09658	-0.20152	-2.89369	-1.87504	-3.91235	-2.69885	-1.74879	-3.64892
Yemen	-0.16477	-0.10677	-0.22278	-2.95746	-1.91636	-3.99856	-2.88005	-1.86619	-3.8939
Zambia	0.060942	0.039489	0.082395	-3.3312	-2.15853	-4.50386	-3.2075	-2.07838	-4.33663
Zimbabwe	0.279197	0.180912	0.377481	0.862734	0.559029	1.166439	0.811967	0.526133	1.0978

4. Discussion

Over the past 30 years, the global prevalence of pediatric thalassemia has decreased. However, due to increasing medical and social costs, pediatric thalassemia remains a significant public health issue. This study investigated the prevalence, thalassemia-related mortality, and thalassemia-related DALYs among children aged 0 to 14 years in all GBD regions and countries from 1990 to 2021. Our findings provide insights into the burden of pediatric thalassemia in regions and countries with different levels of development over the past 30 years.

From 1990 to 2021, both the number of thalassemia-related deaths and the number of thalassemia-related disability-adjusted life years (DALYs) in children decreased. However, the prevalence increased in low and lower-middle SDI

regions, indicating that these areas still face significant challenges in disease control. This may be related to the lack of medical resources, weak public health infrastructure, and insufficient health education in these regions. Additionally, we found a significant negative correlation between SDI and the prevalence, thalassemia-related mortality, and thalassemia-related DALYs. The largest decrease in thalassemia-related mortality in children was observed in high SDI regions, which may be associated with better medical services in these areas, leading to early diagnosis and better treatment of pediatric thalassemia.

Thalassemia is a complex, multifactorial disease influenced by various genetic, metabolic, and environmental factors [10] [11]. The exact role of each factor in pediatric thalassemia is not yet clear and requires further exploration, which may vary by geographic location. These differences in potential factors are related to regional variations in the prevalence and mortality of pediatric thalassemia. Changes in modern dietary patterns have led to a rapid increase in global obesity rates, and obesity is considered a major risk factor for thalassemia and its complications [12]-[14]. Therefore, proactive obesity prevention and dietary management can help slow the progression of pediatric thalassemia.

In children with thalassemia, signs and symptoms are sometimes nonspecific [15]-[17]; delays in diagnosis can have devastating effects on the child's health. Children with thalassemia typically initially present with fatigue, weakness, or symptoms of anemia [18]-[20]. Notably, symptoms of anemia are the primary cause of death in thalassemia patients. Therefore, failure to identify high-risk patients and provide timely treatment can lead to adverse outcomes and high mortality rates, especially in low-income countries. This failure may partially explain why pediatric thalassemia-related mortality is lower in higher SDI regions compared to lower SDI regions. Additionally, cardiovascular diseases can also contribute to the mortality of children with thalassemia [21] [22]. For example, chronic anemia can lead to early and progressive atherosclerosis [23].

Based on the survey results, we propose more specific and actionable policy recommendations, including promoting thalassemia screening programs and public awareness activities in low SDI regions, increasing investment in healthcare resources and improving infrastructure, providing training for healthcare professionals, establishing economic support policies, promoting genetic counseling services, and enhancing international cooperation and aid. These measures aim to improve early detection rates and public awareness of thalassemia, thereby effectively reducing the disease burden in low SDI regions.

5. Limitations

This study has certain limitations. Although the GBD database provides extensive data, it relies on the reporting and data collection quality of individual countries. Data from some regions may be incomplete or inaccurate, affecting the reliability of the results. Secondly, this study uses a cross-sectional design, which cannot establish causality. While trends can be observed, the specific reasons for these

trends cannot be determined.

6. Conclusions

This study reveals the trends and burden of pediatric thalassemia by analyzing epidemiological data at global, regional, and national levels from 1990 to 2021. Although the prevalence, mortality, and disability-adjusted life years (DALYs) of pediatric thalassemia have decreased globally, significant differences remain between regions and countries with different Socio-demographic Index (SDI) levels.

The burden of pediatric thalassemia has significantly decreased in high SDI regions, indicating substantial progress in disease prevention and control in these areas. However, the prevalence and disease burden have increased in low and lower-middle SDI regions, suggesting that these areas still need to strengthen medical resources, public health infrastructure, and health education.

This study emphasizes the importance of enhancing the understanding of the epidemiology of pediatric thalassemia globally. Future research should further explore the specific needs of low SDI regions and develop effective interventions to reduce the disease burden. Additionally, policymakers and public health workers should focus on regional differences and formulate targeted public health policies and resource allocation strategies to better prevent and control pediatric thalassemia.

In conclusion, this study provides important reference data on the epidemiology of pediatric thalassemia at global, regional, and national levels. These data are crucial for the formulation of public health policies and resource allocation, helping to better prevent and control pediatric thalassemia worldwide.

Credit Authorship Contribution Statement

Yongle Li: Writing—review & editing, Writing—original draft, Methodology, Formal analysis, Data curation, Conceptualization. Wanshuo Wei, Yuan Gan, Xiaomei Xie, Pengtao Qin, Liangsen Teng: Writing—review & editing, Writing—original draft, Validation, Methodology, Conceptualization. Lihe Jiang: Conceptualization, Funded this research, Writing—review & editing, Writing—original draft, Formal analysis.

Funding

This study was supported by the Grant of research project on high-level talents of Youjiang Medical College for Nationalities (Grant No. YY2021SK02); Key Laboratory of Pollution Exposure and Health Intervention of Zhejiang Province (Grant No. 202300011).

Acknowledgements

We are grateful to the Global Burden of Disease (GBD) Study team for providing access to the comprehensive database used in this analysis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Shahmirzalou, P., Hamze, M.S. and Sadagheyani, H.E. (2024) A New Formula Based on Simple Blood Indices to Differentiate Beta Thalassemia Trait from Iron Deficiency Anemia. *Iranian Journal of Public Health*, **53**, 1192-1199. <https://doi.org/10.18502/ijph.v53i5.15601>
- [2] Saeidnia, M., Shadfar, F., Sharifi, S., Babashahi, M., Ghaderi, A. and Shokri, M. (2024) Skin Complications during Iron Chelation Therapy for Beta-Thalassemia: Overview and Treatment Approach. *International Journal of Hematology*, **120**, 271-277. <https://doi.org/10.1007/s12185-024-03825-w>
- [3] Banjade, P. and Bhandari, J. (2020) A Child Lost to Follow up Carrying Beta Thalassemia Major: A Case Report. *Journal of Nepal Medical Association*, **58**, 436-438. <https://doi.org/10.31729/jnma.5129>
- [4] Avraham, K., Benjamin, W., Elizabeth, Y., *et al.* (2023) Association and Risk Factors of Pediatric Pulmonary Hypertension with Obstructive Sleep Apnea: A National Study Utilizing the Kids' Inpatient Database (KID). *International Journal of Pediatric Otorhinolaryngology*, **175**, Article ID: 111750.
- [5] Lan, X., Ye, Z., Du, J., Liu, L., Tian, C., Huang, L., *et al.* (2024) Cross-Sectional Study on the Impact of Cardiac and Hepatic Iron Overload, as Measured by MRI T2*, on the Quality of Life in Children with Severe Beta-Thalassemia Major. *Medicine*, **103**, e38817. <https://doi.org/10.1097/md.00000000000038817>
- [6] Babar, S. and Saboor, M. (2024) Erythroferrone in Focus: Emerging Perspectives in Iron Metabolism and Hematopathologies. *Blood Science*, **6**, e00198. <https://doi.org/10.1097/bs9.0000000000000198>
- [7] GBD Diseases and Injuries Collaborators (2024) Global Incidence, Prevalence, Years Lived with Disability (YLDs), Disability-Adjusted Life-Years (DALYs), and Healthy Life Expectancy (HALE) for 371 Diseases and Injuries in 204 Countries and Territories and 811 Subnational Locations, 1990-2021: A Systematic Analysis for the Global Burden of Disease Study 2021. *The Lancet*, **403**, 2133-2161.
- [8] GBD 2019 Diseases and Injuries Collaborators (2020) Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990-2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *The Lancet*, **396**, 1204-1222.
- [9] GBD 2013 Mortality and Causes of Death Collaborators (2015) Global, Regional, and National Age-Sex Specific All-Cause and Cause-Specific Mortality for 240 Causes of Death, 1990-2013: A Systematic Analysis for the Global Burden of Disease Study 2013. *The Lancet*, **385**, 117-171.
- [10] Ding, Q., Liu, S., Yao, Y., Liu, H., Cai, T. and Han, L. (2022) Global, Regional, and National Burden of Ischemic Stroke, 1990-2019. *Neurology*, **98**, e279-e290. <https://doi.org/10.1212/wnl.00000000000013115>
- [11] Glenthøj, A., van Beers, E.J., van Wijk, R., Rab, M.A.E., Groot, E., Vejstrup, N., *et al.* (2024) Designing a Single-Arm Phase 2 Clinical Trial of Mitapivat for Adult Patients with Erythrocyte Membranopathies (SATISFY): A Framework for Interventional Trials in Rare Anaemias—Pilot Study Protocol. *BMJ Open*, **14**, e083691. <https://doi.org/10.1136/bmjopen-2023-083691>
- [12] Padeniya, P. and Premawardhena, A. (2024) Obesity, Liver Steatosis and Metabolic Syndrome: The Hidden Enemies in Transfusion-Dependent Thalassemia. *British*

- Journal of Haematology*, **205**, 28-29. <https://doi.org/10.1111/bjh.19532>
- [13] Stella, S., Stefano, A., Annalisa, N., *et al.* (2022) Survival and Late Effects of Hematopoietic Cell Transplantation in Patients with Thalassemia Major. *Bone Marrow Transplantation*, **57**, 1689-1697. <https://doi.org/10.1038/s41409-022-01786-4>
- [14] Alizadeh, S.R. and Ebrahimzadeh, M.A. (2022) O-substituted Quercetin Derivatives: Structural Classification, Drug Design, Development, and Biological Activities, a Review. *Journal of Molecular Structure*, **1254**, Article ID: 132392. <https://doi.org/10.1016/j.molstruc.2022.132392>
- [15] Sherief, L.M., Goneim, E., Kamal, N.M., Ibraheim, A., Alsolfiani, F. and Alawur, A. (2020) Acute Lymphoblastic Leukemia in a β -Thalassemia Intermedia Child: A Case Report. *World Journal of Clinical Pediatrics*, **9**, 1-6. <https://doi.org/10.5409/wjcp.v9.i1.1>
- [16] Molavi, N., Ghaderi, A. and Banafshe, H. (2020) Determination of Thallium in Urine, Blood, and Hair in Illicit Opioid Users in Iran. *Human & Experimental Toxicology*, **39**, 808-815. <https://doi.org/10.1177/0960327120903487>
- [17] Mudiyanse, R., Dayasiri, M. and Kulathilake, A. (2019) G409(P) Perceptions of Beta Thalassemia Major Patients and Their Parents about Medical Students' History Taking Behaviour. *Archives of Disease in Childhood*, **104**, A166. <https://doi.org/10.1136/archdischild-2019-rcpch.394>
- [18] Domenica, M.C., Antonis, K., *et al.* (2022) Luspatercept for the Treatment of Anaemia in Non-Transfusion-Dependent β -Thalassaemia (BEYOND): A Phase 2, Randomised, Double-Blind, Multicentre, Placebo-Controlled Trial. *The Lancet. Haematology*, **9**, e733-e744.
- [19] Pahuja, S. and Mandal, P. (2024) Alloimmunization and Autoimmunization among Multitransfused Thalassemia and Sickle Cell Disease Patients. *Pediatric Hematology Oncology Journal*, **9**, 200-206. <https://doi.org/10.1016/j.phoj.2024.06.002>
- [20] Lu, D., Gong, X., Guo, X., Cai, Q., Chen, Y., Zhu, Y., *et al.* (2024) Gene Editing of the Endogenous Cryptic 3' Splice Site Corrects the RNA Splicing Defect in the B⁶⁵⁴-Thalassemia Mouse Model. *Human Gene Therapy*, **35**, 825-837. <https://doi.org/10.1089/hum.2023.202>
- [21] Pistoia, L., Meloni, A., Positano, V., Longo, F., Borsellino, Z., Spasiano, A., *et al.* (2024) Multiparametric Cardiac Magnetic Resonance Assessment in Sickle Beta Thalassemia. *Diagnostics*, **14**, Article No. 691. <https://doi.org/10.3390/diagnostics14070691>
- [22] Ali, Z.P., Kumar, M.G., Alina, S., *et al.* (2023) Calcium Channel Blockers for Preventing Cardiomyopathy Due to Iron Overload in People with Transfusion-Dependent Beta Thalassaemia. *The Cochrane Database of Systematic Reviews*, **11**, CD011626.
- [23] Cannon, E.J., Misialek, J.R., Buckley, L.F., Aboelsaad, I.A.F., Ballantyne, C.M., Leister, J., *et al.* (2024) Anemia, Iron Deficiency, and Cause-Specific Mortality: The Atherosclerosis Risk in Communities Study. *Gerontology*, **70**, 1023-1032. <https://doi.org/10.1159/000539973>