LETTER TO THE EDITOR

Global shifts in transfusion-dependent thalassemia (TDT): Epidemiological trends, regional disparities, and prevention strategies (pre-2010 vs. 2015–2021)

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To the editor,

β-transfusion-dependent thalassemia (β-TDT), continues to have a substantial global healthcare impact. Over the past 20 years, increased screening, migration, and better healthcare infrastructure have changed the prevalence of this disease, which has historically been endemic in the Mediterranean Middle East and South/Southeast Asia. We examine the differences between pre-2000 historical estimates and 2015–2021 data from several nations (1-17). Table 1 highlights striking regional disparities in β-thalassemia major prevalence. It shows a marked decline in β-thalassemia prevalence in countries with effective prevention programs, such as Cyprus, Greece, Italy, and Thailand. In contrast, South Asia (India, Pakistan, Bangladesh, Myanmar, Nepal) continues to report high prevalence and large annual affected births, reflecting gaps in nationwide screening. In Western Europe and North America, overall prevalence remains low, but registry data indicate increases due to migration from endemic regions. These patterns highlight both the success of comprehensive programs in reducing incidence and the emerging global impact of migration on disease distribution.

Data summarize changes between pre-2010 historical estimates and post-2015 reports, highlighting marked declines in settings with long-standing prevention programs and persistent high burden in South Asia and parts of Southeast Asia (Figure 1). In several low-prevalence regions, increasing registry estimates are consistent with migration from endemic countries.

Carrier prevalence declined in Mediterranean countries following implementation of structured prevention programs (screening, counseling, prenatal diagnosis), remained relatively stable in several endemic South Asian settings, and showed small increases in some non-endemic regions consistent with migration-related population change. (3–5,10,15,17).

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Table 1. Global burden of transfusion-dependent β-thalassemia (β-TDT): prevalence trends, registry-based estimates, and annual affected births across selected countries/regions.

Country/Region	Prevalence (%) pre-2010	Prevalence (%) 2015–2021	Prevalence per 100,000 (Post-2015)	Estimated Annual Births
Cyprus (3,5,17)	0.63	0.08	–	–
Greece (4,14)	0.85	0.30	25.2	–
Iran (national) (5,16)	2.5 / 1,000 births	0.8 / 1,000 births	–	–
Iran (Fars province)	–	–	32.6	–
Iraq (Najaf province) (5,10)	–	–	49.6	–
India (2,4,5)	0.9	0.6	–	~12,500
Pakistan (2,4,5)	1.2	1.1	–	–
Bangladesh (4,10)	–	–	–	~9,100
Thailand (5,9)	1.0	0.5	–	~4,000
Myanmar (4.9)	–	–	–	~2,500
Nepal (4.9)	–	–	–	~120
China (4,5,7)	0.9	0.7	–	–
Saudi Arabia (5,10)	–	–	23.6	–
Malaysia (4,9)	–	–	18.9	–
Italy (national) (5,13)	0.80	0.20	11.6 (combined)	–
United Kingdom (11,15)	0.02	0.06	–	–
England (registry) (11,15)	–	–	2.3	–
France (13,15)	–	–	0.8 (transfusion-dependent)	–
Germany (13,15)	–	–	0.8	–
Denmark (15)	–	–	1.1	–
Spain (13,15)	–	–	0.2	–
US (4,5,15)	–	–	0.6–0.8	–
North Africa (4,5,10)	0.5	0.6	–	–
Brazil (4,5)	0.05	0.07	–	–

In summary:

The implementation of universal carrier screening, premarital counseling, and prenatal diagnostic programs has resulted in a notable decrease in β-thalassemia major births in Mediterranean nations like Cyprus, Greece, Italy, and Iran. India and Pakistan, on the other hand, continue to report moderately high disease prevalence primarily as a result of high rates of consanguinity, limited access to premarital screening, and deficiencies in public health infrastructure. Even though the incidence of disease is on the decline in Southeast Asian nations like Thailand and China, the sheer size of their populations results in a persistent absolute burden of afflicted people. Meanwhile, mainly due to immigration from endemic areas, new thalassemia clusters are emerging in Northern Europe and Latin America, which have historically been thought of as low-prevalence regions. Recent trends indicate a moderate but increasing burden of thalassemia in North Africa, particularly in nations like Egypt. This is especially true in underserved and rural areas where access to screening and healthcare is still restricted. To address the changing global distribution of β-thalassemia major, these regional

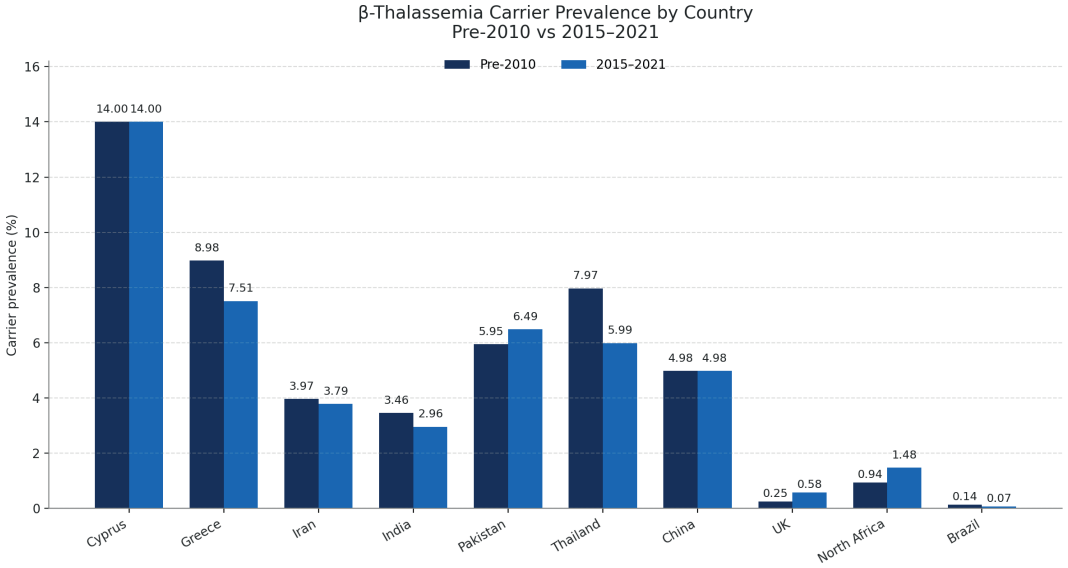

Figure 1. β-thalassemia carrier prevalence before 2010 and in 2015–2021 across selected countries.

disparities underscore the continued need for specialized prevention strategies and reinforced national policies. The prevalence of the β-thalassemia carrier state varies greatly around the world, from less than 1 percent in non-endemic areas to over 10–14 percent in South Asia, the Mediterranean, and the Middle East. Cyprus, Greece, Italy, and Pakistan report some of the highest carrier rates. In Italy, especially in Sardinia and the southern regions, rates can reach 13 percent; however, affected births have been significantly decreased by national prevention programs. Although Northern Europe and the Americas exhibit lower rates, but are seeing increases as a result of immigration from high-prevalence areas, India, Iran, and Thailand continue to maintain intermediate prevalence. This highlights the need for more comprehensive screening and genetic counseling strategies even in populations that are typically low risk. Mediterranean nations with well-established national programs that include universal carrier screening, premarital counseling, and easily accessible prenatal diagnostics, like Cyprus, Greece, and Italy, have effectively decreased the incidence of affected births. These tactics work well as models in areas with high prevalence. On the other hand, because of high rates of consanguinity, low awareness, and poor public health infrastructure, South Asian nations like India and Pakistan still face a heavy disease burden. This highlights the urgent need for funding for community-based screening, widespread education, and reasonably priced genetic services. Although prevalence rates are falling in Southeast Asia, especially in Thailand and China, the sheer volume of cases is still high because of the region's large population, which calls for ongoing efforts at preconception and school-based screening. The moderately increasing prevalence in North Africa, particularly in Egypt, is frequently found in rural and underserved areas, highlighting the significance of decentralizing services and incorporating thalassemia screening into primary healthcare. As a result of migration from endemic countries, low-prevalence regions like Northern Europe and Latin America are now witnessing the emergence of thalassemia clusters. This underscores the necessity of modifying current screening programs and offering targeted genetic counseling to communities that are at risk. National health systems must adapt prevention strategies to their local context to address the changing global distribution of β-thalassemia major. This includes combining culturally sensitive counseling, premarital or antenatal screening, and community education to effectively reduce disease incidence and improve long-term outcomes.

Conflicts of interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted letter to the Editor.

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