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Causes of Hospitalizations in Pediatric Patients with Thalassemia under the National Health Coverage Scheme in Thailand

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Abstract: Thalassemia is a hereditary hemolytic anemia that is prevalent in Southeast Asia. The primary treatment for severe thalassemia involves red cell transfusion, iron chelation, and the treatment of long-term complications, leading to frequent hospital visits and admissions. This study aims to delineate the causes and characteristics of hospital admissions among thalassemia patients under the National Health Coverage (NHC) scheme in Thailand. This cross-sectional analysis (2015–2019), conducted using the National Health Security Office database, identified 336,054 admissions among 41,237 patients, with alpha-thalassemia at 12.5%, beta-thalassemia at 61.5%, other thalassemia at 0.5%, and unclassified thalassemia at 25.5%. The overall admission rate was 3.74 per 100 NHC admissions in the pediatric age group. Infections predominated in younger patients, whereas cardiac complications, diabetes mellitus, and cholecystitis/cholelithiasis were more common in older patients. Hospital admissions for cardiac complications and diabetes mellitus in pediatric patients with thalassemia decreased over the study period. The annual hospital admission cost ranged from 8.19 to 12.01 million US dollars, with one-third attributed to iron chelation. In summary, thalassemia poses a significant healthcare challenge in Thai children, characterized by high admission rates and costs. While infections predominate in younger patients, cardiac complications and diabetes mellitus are more common in older individuals. The diminishing admissions for these complications suggest the successful implementation of iron chelation medications.

Keywords: complications; hospitalization; iron chelation; thalassemia

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1. Introduction

Thalassemia and hemoglobinopathies are the most common inherited hemolytic anemias globally and are highly prevalent in Southeast Asian countries, including Thailand. Thalassemia is caused by mutations of globin genes, resulting in an imbalanced globin synthesis and ineffective erythropoiesis [1]. The main types of thalassemia diseases in the Thai population are homozygous beta-thalassemia, beta-thalassemia/hemoglobin (Hb) E disease, and Hb H disease. The frequency of alpha-thalassemia carriers and beta-thalassemia carriers in the population is approximately 20–30% and 3–9%, respectively.

Hb E, a common Hb variant in the region, has a prevalence ranging from 10% to 53%. Additionally, the prevalence of Hb Constant Spring, a common non-deletional alpha-thalassemia, is estimated to be between 1% and 8% [2]. Thalassemia diseases can be classified by the need for transfusion into transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT) [3]. The primary treatments for TDT are regular red cell transfusion, iron chelation, and the monitoring and treatment of long-term complications. Thalassemia can be cured with stem cell transplantation [3]. Gene therapy has emerged as a curative treatment for thalassemia [4–6]. Treatments for NTDT are on-demand blood transfusions, Hb F stimulation, iron chelation, and may include splenectomy [7]. The cost of treatment in thalassemia is high and contributes to a significant healthcare burden in endemic regions [8–13]. In Western countries, the estimated treatment expenses are generally higher [14,15]. Among patients with TDT, the primary factors contributing to these costs are blood transfusions and iron chelation.

Several disease-related complications have been observed in patients with TDT and NTDT. A multicenter study in 433 adults and adolescents with thalassemia disease in Thailand showed that the prevalence of disease-related complications in patients with TDT and NTDT was 100% and 58.8%, respectively. The common complications included iron overload-related complications, heart failure, pulmonary artery hypertension, extramedullary hematopoiesis, infections, diabetes mellitus, and hypothyroidism [16]. These complications may necessitate hospitalization and lead to a decreased survival of patients with thalassemia.

This study aims to assess the admission rate, co-diagnoses, and cost of hospital admission in pediatric patients across all types of thalassemia disease under the National Health Coverage (NHC) scheme in Thailand. The findings will serve as a foundational understanding of thalassemia-related health challenges in the country, guiding the development of preventive measures to mitigate severe complications in affected individuals.

2. Materials and Methods

The study protocol was granted exemption from review by the Research Ethics Committee of Faculty of Medicine, Chiang Mai University (Study number 8288/2021), and the informed consent was waived because the de-identified data used in the study were obtained with the approval of the National Health Security Office (NHSO) in Thailand, the government organization overseeing the NHC. The research could not practicably be carried out without the waiver of informed consent due to the large population size. This cross-sectional study focused on pediatric patients with thalassemia disease who were hospitalized under the Thailand NHC scheme during the fiscal years 2015–2019 (from 1 October 2014 to 30 September 2019). Data were obtained from the NHSO database, including patients with both principal and co-diagnoses of thalassemia. Thalassemia diagnoses were classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th version (ICD-10): alpha-thalassemia (D56.0); beta-thalassemia (D56.1); other thalassemias (D56.8); thalassemia, unspecified (D56.9) [17]. Age categorization included five groups: birth–1, 1–6, 6–11, 11–16, and 16–18 years.

Hospital admission numbers were analyzed by thalassemia type, fiscal year, and age group. Admission rates were calculated based on NHC admissions (number of thalassemia patient admissions/100 NHC admissions) and the total NHC population in the respective age group (number of thalassemia patient admission/100,000 NHC population).

The causes of admission were analyzed over time and by age group, with infections categorized into intestinal infectious diseases (A00–A09), arthropod-borne viral fevers and viral hemorrhagic fevers (A90–A99), respiratory infections (J00–J06, J09–J18, and J20–J22), and other infections (other codes of A and all B). Additional comorbidities were grouped as heart failure (I50), arrhythmias (I44–I49), other cardiovascular diseases (other codes of I), cholelithiasis (K80), cholecystitis (K81), disorder of iron metabolism, hemochromatosis (E83.1), and diabetes mellitus (E10–E14). All other codes were classified as other comorbidities. The D58.2 code (hemoglobinopathy) was excluded from co-diagnoses, as it

overlapped with the principal diagnosis of thalassemia. Treatments were identified using ICD 9-CM codes 99.04 (transfusion of packed cells) and 99.16 (injection of antidote) for blood transfusion and iron chelation, respectively [17].

The cost of hospital admission, in Thai baht, was collected annually. The cost of hospital admission for iron chelation was calculated from admissions with the diagnosis of disorder of iron metabolism, hemochromatosis (E381), and treatment code 99.16.

3. Results

The analysis revealed data from 41,237 patients with thalassemia diseases who were hospitalized under the NHC scheme in Thailand during the fiscal years 2015–2019. In total, there were 336,054 hospital admissions, with a slight disparity in the number of thalassemia diagnoses compared to admissions due to a minority of patients receiving more than one thalassemia diagnoses.

Alpha-thalassemia accounted for 12.5% (42,101 admissions), beta-thalassemia for 61.5% (206,709 admissions), other thalassemia for 0.5% (1846 admissions), and unclassified thalassemia for 25.5% (85,761 admissions). The admission rates, detailed by thalassemia type and fiscal year, are presented in Table 1. The overall admission rate was 3.74 per 100 NHC admissions, equating to 416–559 admissions per 100,000 population. An upward trend in admission rates was observed from 2015 to 2019, as shown in Figure 1.

Table 1. Admission Rates of Pediatric Patients with Thalassemia Disease Under National Health Coverage (NHC) Scheme Across Fiscal Years.

	Fiscal Year					
Diagnosis by ICD10 *	**2015**	**2016**	**2017**	**2018**	**2019**	**Total**
D560 Alpha-thalassemia	5739	6991	8479	9420	11,472	42,101
D561 Beta-thalassemia	34,677	37,875	42,722	44,528	46,907	206,709
D568 Other thalassemias	314	465	360	382	325	1846
D569 Thalassemia, unspecified	18,092	18,883	17,538	15,357	15,891	85,761
Total diagnosis	58,822	64,214	69,099	69,687	74,595	336,417
Total admissions	58,753	64,144	69,021	69,599	74,537	336,054
Total (person)	15,055	16,403	15,909	15,425	15,798	41,237
Total NHC admission	1,743,869	1,857,172	1,764,712	1,838,505	1,788,952	8,993,210
Number of population	14,128,228	13,904,284	13,730,927	13,529,812	13,339,906	-
Rate/100 admissions	3.37	3.45	3.91	3.79	4.17	3.74
Rate/100,000 population	416	461	503	514	559	-

* ICD10: International Statistical Classification of Diseases and Related Health Problems, 10th version.

The admission rates, categorized by age group, are presented in Table 2, ranging from 0.01 to 11.39 per 100 NHC admissions. Notably, the highest admission rate was observed in the 11–16 years age group. The overall admission rate was 3.74 per 100 NHC admissions in the pediatric age group.

Co-diagnoses recorded during hospital admissions, according to fiscal year, are detailed in Table 3. Out of a total of 336,054 admissions, 163,868 (48.8%) featured at least one co-diagnosis. Hemochromatosis (30.0%) and infections (13.6%) emerged as the most prevalent co-diagnoses. Respiratory infections constituted the majority within the infection category, representing about two-thirds of all infections. Given that some patients received multiple infection diagnoses, the total count slightly exceeded the number of admissions. Over the 5-year study period, the total number of admissions exhibited an upward trajectory. Hemochromatosis diagnoses steadily increased, whereas admissions for iron overload-related complications such as cardiac complications and diabetes mellitus demonstrated a declining trend over time.

Table 2. Admission Rates of Pediatric Patients with Thalassemia Disease Under National Health Coverage (NHC) Scheme Categorized by Age Group.

	Age					
Diagnosis by ICD10 *	**0–1 y**	**1–6 y**	**6–11 y**	**11–16 y**	**16–18 y**	**Total**
D560 Alpha-thalassemia	86	681	13,294	22,246	5794	42,101
D561 Beta-thalassemia	78	1218	48,638	109,162	47,613	206,709
D568 Other thalassemias	3	48	568	859	368	1846
D569 Thalassemia, unspecified	89	2539	25,589	36,453	21,091	85,761
Total diagnosis	256	4486	88,089	168,720	74,866	336,417
Total admissions	256	4484	87,992	168,530	74,792	336,054
Total (person)	246	2881	16,930	16,703	12,059	41,237
Total NHC admission	2,899,951	782,382	2,626,135	1,480,226	1,204,516	8,993,210
Rate/100 admissions	0.01	0.57	3.35	11.39	6.21	3.74

* ICD10: International Statistical Classification of Diseases and Related Health Problems, 10th version.

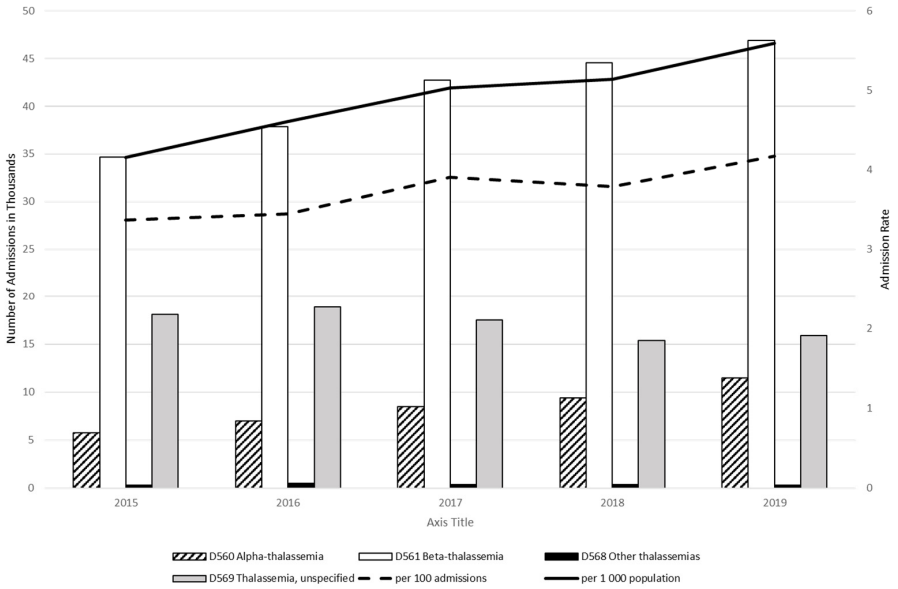

Figure 1. An Upward Trend in Admission Rates of Pediatric Patients with Thalassemia Disease Under National Health Coverage (NHC) Scheme Across Fiscal Year.

Table 3. Co-Diagnoses During Hospital Admission for Pediatric Patients with Thalassemia Disease Across Fiscal Years.

	Fiscal Year					
Co-Diagnoses	**2015**	**2016**	**2017**	**2018**	**2019**	**Total**
Infections	8423	10,078	9555	8846	8736	45,638
-Respiratory infections	5468	6999	6791	5967	5380	30,605
-Intestinal infectious diseases	1444	1714	1607	1617	1520	7902
-Arthropod-borne	762	615	412	618	1055	3462
-Other infections	1326	1445	1327	1181	1350	6629
Heart failure/Arrhythmias	174	172	127	110	101	684
Other cardiovascular diseases	364	459	360	338	318	1839
Cholelithiasis/Cholecystitis	183	196	210	202	242	1033
Diabetes mellitus	51	38	38	24	21	172
Blood transfusion	124	164	146	175	199	808
Hemochromatosis	13,641	16,704	21,614	23,473	25,530	100,962
Other	10,962	11,345	11,623	10,809	11,109	55,848
Total co-diagnosis	34,499	39,851	44,255	44,514	46,825	209,944
Total admissions	58,753	64,144	69,021	69,599	74,537	336,054

Co-diagnoses during hospital admissions, stratified by age group, are presented in Table 4. Infections were more common in younger patients, while cardiac complications, diabetes mellitus, and cholecystitis/cholelithiasis were more common in older patients (11–18 years old) than younger patients (birth–11 years old).

Table 4. Co-Diagnoses During Hospital Admission for Pediatric Patients with Thalassemia Disease Stratified by Age Group.

	Age					
Co-Diagnoses	**0–1 y**	**1–6 y**	**6–11 y**	**11–16 y**	**16–18 y**	**Total**
Infections	16	2179	19,548	16,798	7097	45,638
-Respiratory infections	11	1352	14,531	11,154	3557	30,605
-Intestinal infections	2	841	3631	2331	1097	7902
-Arthropod-borne	-	24	508	1800	1130	3462
-Other infections	4	397	2228	2325	1675	6629
Heart failure/Arrhythmias	3	13	126	221	321	684
Other cardiovascular diseases	5	33	279	755	767	1839
Cholelithiasis/Cholecystitis	-	-	20	383	630	1033
Diabetes mellitus	1	1	8	19	143	172
Blood transfusion	-	16	286	324	182	808
Hemochromatosis	2	36	16,983	59,120	24,821	100,962
Other	230	1403	14,779	23,919	15,517	55,848
Total co-diagnosis	258	4116	53,379	102,351	49,840	209,944
Total admissions	256	4484	87,992	168,530	74,792	336,054

The cost associated with hospital admissions across fiscal years is detailed in Table 5. The median cost per admission was 2994.5 baht (IQR 2225–4520 baht).

Table 5. The cost of hospital admission of pediatric patients with thalassemia disease in National Health Coverage (NHC) by fiscal year.

	Fiscal Year					
Cost of Hospital Admission	**2015**	**2016**	**2017**	**2018**	**2019**	**Total**
Total cost of hospital admission (×1 million baht)	281.8	309.3	338.8	340.2	375.1	1645.1
Total cost of hospital admission for iron chelation (×1 million baht) (% of total cost)	79.2 (28.1)	98.9 (32.0)	124.8 (36.8)	144.8 (42.6)	161.5 (43.1)	609.2 (37.0)

Median cost per admission: 2994.5 baht (IQR 2225–4520 baht).

4. Discussion

This study revealed a high hospital admission rate among pediatric patients with thalassemia under the NHC scheme in Thailand from 2015 to 2019. The admission rate, ranging from 416 to 559 per 100,000, surpassed the rate of 154 per 100,000 observed in a nationwide population-based study across all age groups in Thailand in 2010 [18]. Within this cohort, the highest admission rate occurred in the 11 to 16 years age group, while the lowest was noted in infants. Most hospitalized patients had beta-thalassemia, with hemochromatosis and infections as prominent co-diagnoses. Respiratory tract infections constituted approximately two-thirds of all infections. This study identified a significant presence of cardiovascular complications and diabetes mellitus among patients, underscoring the persistent health challenges associated with iron overload in Thai pediatric patients with thalassemia.

Comparisons with studies from Iran, Sardinia, and Lebanon highlighted similarities in the major complications observed in hospitalized thalassemia patients, such as cardiac com-

plications and diabetes mellitus [19–21]. However, differences were noted, including the absence of mesenteric lymphadenitis associated with desferrioxamine in the current study.

Beazrkar et al. described the causes of hospital admission in 555 patients with beta-thalassemia major at a referral university hospital in Iran from 2000 to 2005. The most common causes of hospital admission were splenectomy, heart failure, liver biopsy, uncontrolled diabetes mellitus, and arrhythmia [19]. Origa et al. described 690 hospital admissions in 276 pediatric and adult patients with thalassemia major in a tertiary care center in Sardinia. The most common causes for hospital admission were heart failure/arrhythmias, infections, mesenteric lymphadenitis in patients treated with subcutaneous desferrioxamine, digestive tract diseases, and liver diseases. Infection was the most common cause of admission in children, whereas heart failure and arrhythmia were the most common cause of admission in patients older than 30 years of age. The rate of patients diagnosed with mesenteric lymphadenitis was noted to decline after 2000–2003. The hospital admissions for other infectious diseases and heart disease also declined during the same period. The author concluded that the increasing use of oral iron chelators influenced the causes of hospital admission [20]. In Thailand, from 2015 to 2017, the first-line iron chelators utilized were desferrioxamine and deferiprone. Oral deferiprone was administered to children aged six years and above. From 2018, under the NHC scheme, deferasirox became the first-line iron chelator for children aged 2 to 6 years old. The prevalent use of oral iron chelators might have reduced the incidence of mesenteric lymphadenitis compared to these earlier studies. Saliba et al. reported 205 admissions in 33 adult patients with thalassemia major and thalassemia intermedia at a tertiary care center in Lebanon over a 20-year period. The most common causes of admission were transfusion therapy, infections, and chemotherapy. Age was a single factor that was associated with a longer hospital stay [21].

The financial implications of thalassemia-related hospital admissions were substantial, with costs ranging from 281.8 to 375.1 million baht or 8.19 to 12.01 million US dollars per year, based on the average yearly currency exchange rate of 31.21–35.46 baht for 1 US dollar (2015–2019 exchange rate) [22]. Notably, one-third of this expense was attributed to the cost of hospital admission for iron chelation, encompassing personnel, facilities, and monthly iron chelator expenses. These findings align with a 2010 population-based study in Thailand, which estimated a total annual healthcare cost of nearly 745 million baht for thalassemia patients, with increasing costs associated with age [18]. Another previous study from three public hospitals in Thailand in children with beta-thalassemia diseases showed that the average annual cost of treatment was 950 USD, in which 59% was direct medical cost, 17% was direct non-medical cost, and 24% was indirect cost. Iron chelator and blood transfusion were the main treatment costs [9]. Over the study period, the diagnosis of hemochromatosis doubled, indicating improved access to medications. Concurrently, admissions for iron overload-related complications, such as cardiac issues and diabetes mellitus, declined. This trend indicates improved awareness of iron overload and its associated complications, resulting in more favorable outcomes.

As this study encompassed all diagnoses of thalassemia, spanning from NTDT to TDT, the low admission rate in infants and young children could indicate patients with milder forms of the disease, such as Hb H disease, which tends to be diagnosed at an older age. This observation may also highlight an existing unmet need. While a successful universal screening program for couples at risk of fetal severe thalassemia diseases, including beta-thalassemia major, beta-thalassemia/Hb E disease, and Hb Bart's hydrops fetalis, has been implemented in Thailand [23], neonatal screening is not currently available. The establishment of universal neonatal screening for thalassemia in Thailand could play a significant role in the early diagnosis of severe thalassemia not screened prenatally, as well as milder forms of thalassemia, and in improved management, leading to better outcomes.

Of note, the information obtained through ICD codes presented limitations in diagnosing thalassemia and classifying its severity. The grouping of beta-thalassemia major and beta-thalassemia/Hb E disease under the same ICD10 codes rendered differentiation impractical. The classification into TDT and NTDT was not possible. Additionally, a notable

percentage consisted of other thalassemias or unspecified thalassemia. The retrospective nature of this study introduced limitations related to data completeness, including the number of hospitalizations from the same patient and the details of co-diagnoses, but the robust sample size enhances the generalizability of the findings, providing valuable insights into the healthcare landscape for pediatric patients with thalassemia in Thailand.

In conclusion, this study underscores the substantial healthcare burden posed by thalassemia in Thai children, emphasizing the need for comprehensive strategies. While infections dominate complications in younger patients, cardiac issues and diabetes mellitus pose significant risks in older children, emphasizing the critical role of iron chelation. The observed decline in admissions for certain complications suggests successful interventions, and the establishment of outpatient transfusion and iron chelation units in primary hospitals is recommended to optimize patient care, reduce healthcare costs, and enhance treatment compliance.

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Data Availability Statement: Data supporting the reported results are not available in a public repository due to privacy restriction.

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References

1. Higgs, D.R.; Thein, S.L.; Wood, W.G. Thalassaemia: Classification, genetics and relationship to other inherited disorders of haemoglobin. In *The Thalassaemia Syndromes*; Weatherall, D.J., Clegg, J.B., Eds.; Blackwell Science: Oxford, UK, 2001; pp. 121–132.
2. Fucharoen, S.; Weatherall, D.J. Progress Toward the Control and Management of the Thalassemias. *Hematol. Oncol. Clin. N. Am.* **2016**, *30*, 359–371. [CrossRef] [PubMed]
3. Anurathapan, U.; Pakakasama, S.; Mekjaruskul, P.; Sirachainan, N.; Songdej, D.; Chuansumrit, A.; Charoenkwan, P.; Jetsrisuparb, A.; Sanpakit, K.; Pongtanakul, B.; et al. Outcomes of thalassemia patients undergoing hematopoietic stem cell transplantation by using a standard myeloablative versus a novel reduced-toxicity conditioning regimen according to a new risk stratification. *Biol. Blood Marrow Transplant.* **2014**, *20*, 2066–2071. [CrossRef] [PubMed]
4. Thompson, A.A.; Walters, M.C.; Kwiatkowski, J.; Rasko, J.E.J.; Ribeil, J.A.; Hongeng, S.; Magrin, E.; Schiller, G.J.; Payen, E.; Semeraro, M.; et al. Gene Therapy in Patients with Transfusion-Dependent beta-Thalassemia. *N. Engl. J. Med.* **2018**, *378*, 1479–1493. [CrossRef] [PubMed]
5. Frangoul, H.; Altshuler, D.; Cappellini, M.D.; Chen, Y.S.; Domm, J.; Eustace, B.K.; Foell, J.; de la Fuente, J.; Grupp, S.; Handgretinger, R.; et al. CRISPR-Cas9 Gene Editing for Sickle Cell Disease and beta-Thalassemia. *N. Engl. J. Med.* **2021**, *384*, 252–260. [CrossRef] [PubMed]
6. Locatelli, F.; Thompson, A.A.; Kwiatkowski, J.L.; Porter, J.B.; Thrasher, A.J.; Hongeng, S.; Sauer, M.G.; Thuret, I.; Lal, A.; Algeri, M.; et al. Betibeglogene Autotemcel Gene Therapy for Non-beta(0)/beta(0) Genotype beta-Thalassemia. *N. Engl. J. Med.* **2022**, *386*, 415–427. [CrossRef] [PubMed]
7. Viprakasit, V.; Ekwattanakit, S. Clinical Classification, Screening and Diagnosis for Thalassemia. *Hematol. Oncol. Clin. N. Am.* **2018**, *32*, 193–211. [CrossRef] [PubMed]

8. Ho, W.L.; Lin, K.H.; Wang, J.D.; Hwang, J.S.; Chung, C.W.; Lin, D.T.; Jou, S.T.; Lu, M.Y.; Chern, J.P. Financial burden of national health insurance for treating patients with transfusion-dependent thalassemia in Taiwan. *Bone Marrow Transplant.* **2006**, *37*, 569–574. [CrossRef] [PubMed]
9. Riewpaiboon, A.; Nuchprayoon, I.; Torcharus, K.; Indaratna, K.; Thavorncharoensap, M.; Ubol, B.O. Economic burden of beta-thalassemia/Hb E and beta-thalassemia major in Thai children. *BMC Res. Notes* **2010**, *3*, 29. [CrossRef] [PubMed]
10. Moirangthem, A.; Phadke, S.R. Socio-demographic Profile and Economic Burden of Treatment of Transfusion Dependent Thalassemia. *Indian J. Pediatr.* **2018**, *85*, 102–107. [CrossRef] [PubMed]
11. Reed-Embleton, H.; Arambepola, S.; Dixon, S.; Maldonado, B.N.; Premawardhena, A.; Arambepola, M.; Khan, J.A.M.; Allen, S. A cost-of-illness analysis of beta-Thalassaemia major in children in Sri Lanka—Experience from a tertiary level teaching hospital. *BMC Pediatr.* **2020**, *20*, 257. [CrossRef] [PubMed]
12. Uchil, A.; Muranjan, M.; Gogtay, N.J. Economic burden of beta-thalassaemia major receiving hypertransfusion therapy at a public hospital in Mumbai. *Natl. Med. J. India* **2023**, *36*, 11–16. [CrossRef] [PubMed]
13. Esmaeilzadeh, F.; Ahmadi, B.; Vahedi, S.; Barzegari, S.; Rajabi, A. Major Thalassemia, Screening or Treatment: An Economic Evaluation Study in Iran. *Int. J. Health Policy Manag.* **2022**, *11*, 1112–1119. [CrossRef] [PubMed]
14. Eleftheriou, A.; Antoniou, E.; Darba, J.; Ascanio, M.; Angastiniotis, M.; Farmakis, D. Estimating the Cost of Thalassemia Care across the World: A Thalassemia International Federation Model. *Hemoglobin* **2022**, *46*, 308–311. [CrossRef] [PubMed]
15. Udeze, C.; Evans, K.A.; Yang, Y.; Lillehaugen, T.; Manjelievskaia, J.; Mujumdar, U.; Li, N.; Andemariam, B. Economic and clinical burden of managing transfusion-dependent beta-thalassemia in the United States. *J. Med. Econ.* **2023**, *26*, 924–932. [CrossRef] [PubMed]
16. Chuncharunee, S.; Teawtrakul, N.; Siritanaratkul, N.; Chueamuangphan, N. Review of disease-related complications and management in adult patients with thalassemia: A multi-center study in Thailand. *PLoS ONE* **2019**, *14*, e0214148. [CrossRef] [PubMed]
17. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*, 10th ed.; World Health Organization: Geneva, Switzerland, 2010. Available online: https://icd.who.int/browse10/2010/en#/ (accessed on 1 January 2022).
18. Teawtrakul, N.; Chansung, K.; Sirijerachai, C.; Wanitpongpun, C.; Thepsuthammarat, K. The impact and disease burden of thalassemia in Thailand: A population-based study in 2010. *J. Med. Assoc. Thai.* **2012**, *95* (Suppl. 7), S211–S216. [PubMed]
19. Bazrgar, M.; Peiravian, F.; Abedpour, F.; Karimi, M. Causes for hospitalization and death in Iranian patients with beta-thalassemia major. *Pediatr. Hematol. Oncol.* **2011**, *28*, 134–139. [CrossRef] [PubMed]
20. Origa, R.; Anni, F.; Mereu, L.; Follesa, I.; Campus, S.; Dessi, C.; Foschini, M.L.; Leoni, G.; Moi, P.; Morittu, M.; et al. Causes of hospital admission in children and adults with transfusion-dependent thalassemia in Sardinia, 2000-2015. *Ann. Hematol.* **2017**, *96*, 1041–1042. [CrossRef] [PubMed]
21. Saliba, A.N.; Moukhadder, H.M.; Harb, A.; Beydoun, H.; Bou-Fakhredin, R.; Taher, A.T. Causes of hospital admission in beta-thalassemia (CHAT) in Lebanon from 1995 to 2015: A pilot retrospective study from a tertiary care center. *Am. J. Hematol.* **2017**, *92*, E652–E653. [CrossRef] [PubMed]
22. Bank of Thailand Daily Foreign Exchange Rates. Available online: https://www.bot.or.th/en/statistics/exchange-rate.html (accessed on 8 December 2023).
23. Tongsong, T.; Charoenkwan, P.; Sirivatanapa, P.; Wanapirak, C.; Piyamongkol, W.; Sirichotiyakul, S.; Srisupundit, K.; Tongprasert, F.; Luewan, S.; Ratanasiri, T.; et al. Effectiveness of the model for prenatal control of severe thalassemia. *Prenat. Diagn.* **2013**, *33*, 477–483. [CrossRef] [PubMed]