Healthcare Resource Utilization Among Patients With Transfusion-Dependent β-Thalassemia in France

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INTRODUCTION

- β-thalassemia is a rare hereditary hemoglobinopathy characterized by reduced or absent β-globin production, leading to ineffective erythropoiesis[1-4]
- The most severe form of the disease is transfusion-dependent β-thalassemia (TDT), wherein patients depend on regular red blood cell transfusions (RBCTs) and iron chelation therapy (ICT) for survival[1,2]
- In addition, patients with TDT experience significant clinical complications that impact all organ systems, requiring substantial healthcare resource utilization (HCRU) to manage the disease[3,5,6]
- There are limited contemporary data on HCRU in patients with TDT in France[5]

OBJECTIVE

- To describe the HCRU of patients with TDT in France

METHODS

Study Design and Database

- A longitudinal, retrospective cohort study design utilized the French National Health Data System database, Système National des Données de Santé (SNDS), to identify patients with TDT in France
- The SNDS is a national claims database that captures pseudonymized, longitudinal data for ~99% of the French population, inclusive of overseas territories and reports claims data for 65 million insurees[7]
  - The SNDS contains details of all primary care, hospital, and pharmacy records reimbursed in France
- The study was conducted from January 1, 2012, to March 1, 2020, and included a 7-year eligibility period (from January 1, 2012, to March 1, 2019) and a minimum follow-up of 1 year after inclusion

Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - An inpatient claim or registration in the long-term disease (LTD) database with a diagnosis of β-thalassemia between January 1, 2012, and March 1, 2019
  - At least 8 RBCTs/year in any 2 consecutive years after the first qualifying β-thalassemia diagnosis record between January 1, 2012, and March 1, 2019
  - At least 12 months of follow-up data after and including the index date
- Patients were excluded if they met the following exclusion criterion:
  - Evidence of sickle cell disease, α-thalassemia, hereditary persistence of fetal hemoglobin, or hematopoietic stem cell transplant at any time in their medical records
- The index date was the date of the eighth RBCT record in the second year of 2 consecutive years
- All patients were followed for at least 12 months from the index date until death or the end of the study period (March 1, 2020)

Study Measures and Analysis

- Descriptive analyses were conducted for demographics and HCRU for patients with TDT
  - Mean (standard deviation [SD]) values were reported for continuous variables and frequencies/proportions (n [%]) for categorical variables
  - In all cases where data were available for <10 patients, values were masked to protect patient confidentiality
- Demographics, including age, sex, and area of residence, were assessed at the index date
- Rates of RBCTs and HCRU (per patient per year [PPPY]) were summarized during follow-up
  - Additionally, descriptive analyses of HCRU during follow-up were conducted for prespecified subgroups

Subgroup Analyses

- Descriptive analyses for HCRU were conducted among 2 subgroups of patients based on the following criteria:
  - RBCT frequency during follow-up (<8, 8–16, and ⩾16 PPPY)
  - Age (years) at the index date (<18 and ⩾18)

RESULTS

Patient Demographics

- A total of 331 patients with TDT were identified in the SNDS database (**Figure 1**)

Figure 1. Patient Attrition[a]

Patients with TDT

Patients with ⩾1 inpatient claim or LTD registration with a β-thalassemia diagnosis in the SNDS between January 1, 2012, and March 1, 2019
N = 9,913

↓

Patients with ⩾8 RBCTs/year in any 2 consecutive years after the first qualifying β-thalassemia claim
N = 474 (4.8%)

↓

⩾12 months of continuous enrollment after and including the index date (eighth RBCT in the second consecutive year)
N = 457 (4.6%)

↓

No evidence of SCD, α-thalassemia, HPFH, or HSCT
N = 331 (3.3%)

HPFH, hereditary persistence of fetal hemoglobin; HSCT, hematopoietic stem cell transplant; LTD, long-term disease; RBCT, red blood cell transfusion; SCD, sickle cell disease; SNDS, Système National des Données de Santé; TDT, transfusion-dependent β-thalassemia.
[a]Values presented in parentheses represent the proportion of total number of patients with ⩾1 inpatient claim or LTD database registration during the study period.

- The mean age of patients with TDT was 26.1 years (SD: 18.0; range: 1–88), and 49.6% of patients were female (**Table 1**)
- Nearly all patients (95%) lived in Metropolitan France, while 3.9% lived in Overseas France (**Table 1**)
- Of the 331 patients, 87% had an LTD registration with a diagnosis of β-thalassemia (**Table 1**)

Table 1. Baseline Demographics

	Patients With TDT (N = 331)
Age, years, mean (SD; range)	26.1 (18.0; 1–88)
Age categories (years), n (%)	
0–11	88 (26.6)
12–35	146 (44.1)
⩾36	97 (29.3)
Female, n (%)	164 (49.6)
Broad area of residence, n (%)	
Metropolitan France	314 (94.9)
Overseas France	13 (3.9)
Unknown	<10
LTD registration, n (%)[a]	309 (93.4)
With β-thalassemia code	289 (87.3)
Follow-up time, years, mean (SD; range)	4.9 (1.9; 1.0–6.9)

LTD, long-term disease; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.
[a]Patients were registered to this database with the corresponding ICD-10 code for the disease that required long-term and/or expensive treatment due to its severity and/or chronic nature.

HCRU

- Patients averaged 13.5 RBCTs and 11.2 ICT claims PPPY during follow-up
- Patients with TDT averaged 16.9 outpatient prescriptions, 14.8 inpatient admissions, 9.7 laboratory tests, 6.3 outpatient visits, and 3.3 emergency room visits PPPY (**Table 2**)
  - Of the 14.8 inpatient hospitalizations PPPY, 13.8 were for <1 day and 1 was for ⩾1 day
  - On average, patients spent 26 total days PPPY in the inpatient hospital setting

Table 2. HCRU

HCRU, Mean Rate PPPY (SD)	Patients With TDT (N = 331)
Outpatient prescriptions	16.9 (7.5)
Inpatient hospital admissions	14.8 (6.1)
Day cases (<1 day)	13.8 (6.1)
Overnight stays (⩾1 day)	1 (2.7)
Total days hospitalized	26 (49.4)
Outpatient laboratory tests	9.7 (9.1)
Outpatient visits	6.3 (4.8)
External consultations at hospital	3.1 (2.8)
Visits outside hospital	3.2 (3.3)
ER visits	3.3 (2.9)
Followed by inpatient admission	0.2 (0.4)
Not followed by inpatient admission	3.1 (2.8)
RBCTs	13.5 (5.2)

ER, emergency room; HCRU, healthcare resource utilization; PPPY, per patient per year; RBCT, red blood cell transfusion; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.

Subgroup Analyses: HCRU

- As the number of RBCTs during follow-up increased, so did HCRU, including inpatient admission rates PPPY (0 to <8 RBCTs: 6.5; 8–16 RBCTs: 13.3; >16 RBCTs: 21.3) (**Table 3**)

Subgroup Analyses: HCRU (Continued)

- Patients in the older age cohort (⩾18 years) compared with the younger age cohort (<18 years) had higher rates of outpatient prescriptions (17.6 vs 15.7), outpatient visits (7.1 vs 4.9), and inpatient admissions (15.5 vs 13.7) (**Table 3**)
  - Inpatient admissions were driven by cases lasting <1 day (14.5 vs 12.5)

Table 3. Subgroup Analyses: HCRU by Number of RBCTs and Age

HCRU, Mean Rate PPPY (SD)	RBCTs PPPY			Age Group	
	<8 (n = 24)	8–16 (n = 223)	>16 (n = 84)	<18 Years (n = 126)	⩾18 Years (n = 205)
Outpatient prescriptions	13.4 (10.3)	16.7 (7.2)	18.5 (7.0)	15.7 (5.9)	17.6 (8.2)
Inpatient admissions	6.5 (6.6)	13.3 (3.2)	21.3 (6.5)	13.7 (5.2)	15.5 (6.5)
Day cases (<1 day)	5.3 (6.9)	12.2 (3.2)	20.4 (6.0)	12.5 (5.0)	14.5 (6.6)
Overnight stays (⩾1 day)	1.2 (2.4)	1.1 (3.1)	0.9 (1.5)	1.2 (4.0)	0.9 (1.6)
Total days hospitalized	18.3 (42.5)	27.4 (58.2)	24.4 (10.5)	31.3 (71.6)	22.7 (27.8)
Outpatient laboratory tests	8.0 (11.0)	7.9 (8.0)	15.0 (9.4)	6.7 (6.4)	11.6 (10.0)
Outpatient visits	4.8 (4.5)	5.9 (4.3)	7.7 (5.7)	4.9 (4.1)	7.1 (5.0)
External consultations at hospital	2.2 (2.2)	2.8 (2.4)	3.9 (3.6)	2.9 (3.3)	3.1 (2.4)
Visits outside hospital	2.6 (3.1)	3.1 (2.9)	3.8 (4.2)	2.0 (1.9)	4.0 (3.8)
ER visits	2.4 (2.4)	3 (2.5)	4.2 (3.7)	3.1 (3.4)	3.4 (2.5)
Not followed by inpatient admission	2.2 (2.2)	2.8 (2.4)	3.9 (3.6)	2.9 (3.3)	3.1 (2.4)
Followed by inpatient admission	0.2 (0.5)	0.2 (0.4)	0.3 (0.4)	0.2 (0.3)	0.2 (0.4)
RBCTs	4.1 (2.3)	12.2 (1.8)	19.7 (5.2)	12.6 (3.9)	14.1 (5.7)

ER, emergency room; HCRU, healthcare resource utilization; PPPY, per patient per year; RBCT, red blood cell transfusion; SD, standard deviation.

LIMITATIONS

- As with any claims study, the use of ICD-10 codes and Classification Commune des Actes Médicaux (CCAM) procedure codes to identify patients could lead to misclassification bias; however, the effect of this bias was limited in this study, given the additional requirements for identifying patients with TDT (e.g., 8 RBCTs/year over 2 consecutive years)
  - HCRU from the actual use of some treatments could have been underestimated, as prescriptions administered during hospital stays were not documented (unless the drugs prescribed were classified as expensive drugs)
- Given the minimum 12-month post-index period for patients with TDT, individuals who died during this period were excluded, which may have further led to an underestimation of HCRU

CONCLUSIONS

- Patients with TDT in France require substantial HCRU driven by the frequent use of RBCTs and ICT, as well as frequent outpatient prescriptions, inpatient admissions, and outpatient visits
- A higher number of RBCTs and older age were associated with higher HCRU
- Elevated HCRU in patients with TDT highlights the need for innovative therapies in this space

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AUTHOR DISCLOSURES

JB, CU, NL and LD are employees of Vertex Pharmaceuticals Incorporated and may hold stock or stock options in the company. LB is a former employee of Vertex Pharmaceuticals and may hold stock or stock options in the company. GP, NQ, and HJ are employees of Certara France and may hold stock or stock options in the company. FG is an employee of the Sickle Cell Referral Center, Henri Mondor Hospital Paris, France. Approval for use of SNDS data was granted by all relevant authorities and governing bodies. Analyses for this study were performed through remote access on the Caisse Nationale de L'assurance Maladie (CNAM) portal to comply with national security guidance (Le Référentiel de Sécurité). The final protocol was reviewed and approved by a scientific committee and the National Informatics and Liberty Commission (CNIL, decision DR-2022-065, March 2, 2022). All patient data were pseudonymized, which according to applicable legal requirements renders the data exempt from privacy laws; therefore, obtaining informed consent from patients was not required. The interpretation and conclusions contained in this study are those of the authors alone.

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