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

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INTRODUCTION

- β-thalassemia is a hereditary hemoglobinopathy characterized by reduced or absent β-globin production, which leads 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 therapies (ICTs) for survival[1,2]
- Patients with TDT have significant complications associated with iron overload that impact all organ systems and lead to significant morbidity, mortality, and healthcare resource utilization (HCRU)[1-4]

OBJECTIVE

- To determine the HCRU among patients with TDT in Italy

METHODS

Study Design and Database

- A longitudinal, retrospective cohort study design was used to identify patients with TDT in an administrative claims database of Italian Local Health Units (LHU), covering 12 million Italian National Health Service health-assisted individuals, from January 1, 2010, to February 1, 2020
  - The demographic, pharmaceutical, hospitalization, outpatient specialist service, and payment exemption databases were included in the LHU database
- The dataset does not contain emergency department (ED) information; therefore, HCRU is likely to be underestimated

Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - At least 1 prescription for ICTs between January 1, 2011, and February 1, 2019
  - Eight or more RBCTs in any 12-month period
  - At least 12 months of data availability before and after the index date (see definition below)
- Patients were excluded if they met the following exclusion criteria:
  - Those with sickle cell disease (SCD), myelodysplastic syndrome, myelofibrosis, iron deficiency anemia, congenital anemias, or myelophthisis
  - Evidence of hematopoietic stem cell transplant at any time in their medical records
  - At least 1 prescription claim for erythropoietin in the inclusion period
- The index date was the date of the first RBCT claim
- All patients were followed for ⩾12 months from index to a censoring event or the end of the study period (February 1, 2020)

Matched Controls

- Each patient with TDT was propensity-score-matched to 5 controls without TDT from the general population of Italy

Matched Controls (Continued)

- Matching was based on the following criteria: age (in years) at index, sex, geographic area (North, Central, or South Italy), and index year
- Matched controls were assumed to have a similar index date as their matched patients
- Matched controls were required to have 12 months of data before and after their index date
- Matched controls were followed for ⩾12 months from index to a censoring event or the end of the study period (February 1, 2020)

Study Measures and Analysis

- Descriptive analyses were conducted for patient demographics and HCRU for patients with TDT and matched controls
  - Mean (standard deviation [SD]) values were reported for continuous variables, and frequencies/proportions (n [%]) were reported for categorical variables
- Demographics, including age, sex, and geographic area, were assessed at index
- The rate of HCRU (per patient per year [PPPY]) was calculated during follow-up
- Comparative analyses were conducted for HCRU between patients with TDT and matched controls; a T-test was used for significance testing ($P<0.05$)

Subgroup Analyses

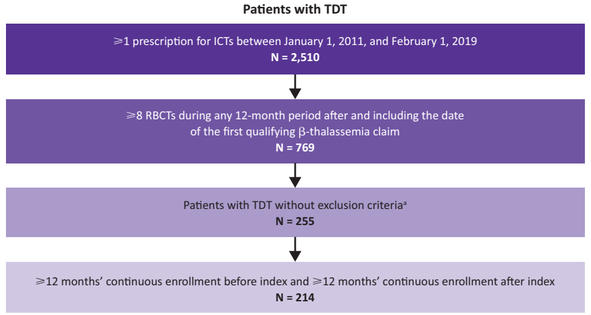
- Subgroup analyses were conducted for HCRU based on patient age at index (0–11 years, 12–35 years, 36–64 years, or ⩾65 years) and the number of RBCTs PPPY during follow-up (<8, 8–16, or >16)

RESULTS

Patient Demographics

- A total of 214 patients with TDT were identified in the LHU administrative claims database and matched to 1,070 controls (**Figure 1**)
- The mean age of patients with TDT was 46.7 years (SD: 20.2), and 54.2% of patients were female (**Table 1**)
- Demographics between patients with TDT and matched controls were similar (**Table 1**)

Figure 1. Patient Attrition



ICT, iron chelation therapy; RBCT, red blood cell transfusion; SCD, sickle cell disease; TDT, transfusion-dependent β-thalassemia.
[a]Exclusion criteria included the following: patients with myelodysplastic syndrome, myelofibrosis, iron deficiency anemia, congenital anemias, myelophthisis, or SCD; evidence of hematopoietic stem cell transplant at any time in their medical records; or ⩾1 prescription claim for erythropoietin in the inclusion period.

Table 1. Baseline Demographics

	Patients With TDT (N = 214)	Matched Controls (N = 1,070)
Age (years), mean (SD)	46.7 (20.2)	45.0 (19.4)
Age categories (years), n (%)		
0–11	7 (3.3)	58 (5.4)
12–35	58 (27.1)	255 (23.8)
36–64	98 (45.8)	542 (50.7)
⩾65	51 (23.8)	215 (20.1)
Sex, n (%)		
Female	116 (54.2)	609 (56.9)
Male	98 (45.8)	461 (43.1)
Geographic area, n (%)		
North Italy	40 (18.7)	186 (17.4)
Central Italy	25 (11.7)	106 (9.9)
South Italy	149 (69.6)	778 (72.7)
Follow-up time (years), mean	4.56 (2.5)	5.6 (2.4)

SD, standard deviation; TDT, transfusion-dependent β-thalassemia.

HCRU

- Patients with TDT averaged 18.18 RBCTs PPPY (SD: 12.2) during follow-up
- Patients with TDT experienced a mean rate of 1.35 hospitalizations, 21.92 outpatient services, and 20.30 prescriptions (all PPPY) during follow-up (**Table 2**)
- Patients with TDT had significantly higher HCRU than matched controls (**Table 2**)

Table 2. HCRU

HCRU, Mean Rate PPPY (SD)	Patients With TDT (N = 214)	Matched Controls (N = 1,070)
All-cause hospitalizations	1.35 (3.4)	0.09 (0.3)*
Day-hospital	0.62 (1.8)	0.02 (0.2)*
Ordinary	0.73 (2.0)	0.06 (0.3)*
Prescriptions	20.30 (12.5)	4.91 (7.7)*
Outpatient services	21.92 (17.0)	1.58 (3.4)*
Diagnostic tests/laboratory visits	10.50 (8.0)	1.12 (2.4)*
Visits	11.41 (13.7)	0.46 (1.4)*

HCRU, healthcare resource utilization; PPPY, per patient per year; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.
**P<0.001 between patients with TDT and matched controls (T-test).*

Subgroup Analysis: HCRU

- As the age of patients with TDT increased, the rate of prescriptions PPPY also increased (aged 0–11 years: 8.19; aged 12–35 years: 14.49; aged 36–64 years: 20.17; aged ⩾65 years: 28.81) (**Table 3**)
- As the number of RBCTs PPPY increased, so did the number of outpatient services PPPY (<8 RBCTs: 13.52; 8–16 RBCTs: 17.75; >16 RBCTs: 27.42)

Table 3. HCRU by Age and RBCTs Subgroup

	Age Subgroups				RBCT Subgroups		
HCRU, Mean Rate PPPY (SD)	0–11 Years (n = 7)	12–35 Years (n = 58)	36–64 Years (n = 98)	≥65 Years (n = 51)	<8 RBCTs (n = 36)	8–16 RBCTs (n = 70)	>16 RBCTs (n = 108)
All-cause hospitalizations	1.90 (2.9)	0.70 (2.0)	0.66 (1.3)	3.34 (5.9)	1.17 (1.9)	1.42 (3.2)	1.36 (3.9)
Day-hospital	1.06 (1.7)	0.54 (1.8)	0.39 (0.7)	1.07 (2.8)	0.73 (1.3)	0.68 (1.9)	0.54 (1.8)
Ordinary	0.85 (1.6)	0.16 (0.4)	0.27 (0.7)	2.27 (3.5)	0.44 (1.0)	0.74 (1.9)	0.82 (2.3)
Prescriptions	8.19 (5.3)	14.49 (8.2)	20.17 (10.4)	28.81 (15.8)	17.69 (11.3)	20.65 (12.1)	20.94 (13.2)
Outpatient services	11.35 (6.3)	18.17 (9.7)	18.97 (11.1)	33.30 (26.5)	13.52 (12.3)	17.75 (13.4)	27.42 (18.6)
Diagnostic tests/ laboratory visits	4.16 (1.4)	8.69 (4.8)	9.62 (6.1)	15.13 (11.9)	7.59 (6.5)	10.09 (8.2)	11.74 (8.1)
Visits	7.20 (6.6)	9.48 (8.4)	9.35 (8.4)	18.17 (22.8)	5.93 (7.5)	7.66 (9.2)	15.68 (16.3)

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

LIMITATIONS

- This study used administrative claims data collected for reimbursement purposes and is therefore subject to potential misclassification bias
- The dataset does not contain ED information; thus, HCRU and burden of disease are likely to be under-reported
- Given the minimum 12-month pre-index and post-index period for patients with TDT, individuals who died or were not continuously enrolled were excluded, which could have led to an underestimation of mortality

CONCLUSIONS

- Patients with TDT had significantly higher HCRU than matched controls from the general population in Italy; although, HCRU is likely to be underestimated, given the lack of ED admissions in the LHU database
- Older age and a higher number of RBCTs were associated with increased outpatient services and prescriptions for patients with TDT
- Elevated HCRU in patients with TDT highlights the needs for innovative therapies in this space

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AUTHOR DISCLOSURES

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