EE287

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

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INTRODUCTION

- β-thalassemia is a rare hereditary hemoglobinopathy characterized by reduced or absent β-globin production, which leads to ineffective erythropoiesis[1-3]
- 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]
- Individuals with TDT experience significant clinical complications that impact all organ systems, especially the hepatobiliary, cardiopulmonary, and endocrine systems, which can lead to healthcare resource utilization (HCRU) and early mortality in this patient population[3]
- There are limited data on HCRU in patients with TDT from comprehensive primary care and secondary care databases in England

OBJECTIVE

- To determine the HCRU among patients with TDT in England

METHODS

Study Design and Database

- A longitudinal, retrospective cohort study design was used to identify patients with TDT in the Clinical Practice Research Datalink (CPRD) linked with the Hospital Episode Statistics (HES) database
  - CPRD Aurum is a large, anonymized, longitudinal source of electronic medical records containing ~13 million registered patients from over 1,375 UK primary care centers
  - HES is a data warehouse containing details of all admissions to National Health Services (NHS) hospitals in England (~168 acute NHS trusts)
    - The HES database contains details of all inpatient admissions, accident and emergency attendances, and outpatient appointments at NHS hospitals in England
- Overall, the study included data from July 1, 2008, to June 30, 2019, and included a 10-year eligibility period (July 1, 2008, to June 30, 2018), as well as a minimal follow-up of 1 year after inclusion (i.e., until June 30, 2019, for patients with an index date at the end of June 2018)

Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - Diagnosis of β-thalassemia between July 1, 2008, and June 30, 2018
  - Eight or more RBCTs per year in ⩾2 consecutive years
  - Registered within the CPRD and eligible for an HES linkage
  - At least 12 months of follow-up data after the index date (see definition below)
- Patients were excluded if they met the following exclusion criteria:
  - Evidence of hematopoietic stem cell transplant, hereditary persistence of fetal hemoglobin, sickle cell disease, or α-thalassemia 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 ⩾12 months from index to a censoring event or the end of the study period (June 30, 2019)

Matched Controls

- Each patient with TDT was exact matched to up to 5 controls without TDT from the general population without replacement
- Matching was based on the following criteria: age (in years) at index (±5 years), sex, geographic region of general practice, and ethnicity
- Matched controls were assigned the same index date as their matched patients

Matched Controls (Continued)

- Matched controls had to be registered within the CPRD at index, to be eligible for an HES linkage, and to have ⩾1 year of follow-up data from the index date
- Matched controls were followed for ⩾12 months from index to a censoring event or the end of the study period (June 30, 2019)

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
  - In all reporting, patient numbers <5 were masked (i.e., reported as "–") to protect patient confidentiality, and secondary masking was applied where required to avoid back-calculation
- Demographics, including age, sex, ethnicity, and socio-economic status, were assessed at index
  - Socio-economic status was calculated using the Index of Multiple Deprivation (IMD) (composite measure of material deprivation including income, employment, education and skills, health, housing, crime, access to services, and living environment) for patients with TDT and matched controls
- The rate of HCRU (per patient per year [PPPY]) was calculated during follow-up
- Comparative analyses were conducted for HCRU between patients and matched controls; a Z-test was used for significance testing ($P<0.05$)

Subgroup Analyses

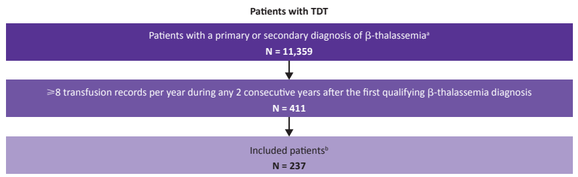
- Two subgroup analyses were conducted for HCRU: age at index (<18 years or ⩾18 years) and number of RBCTs PPPY during follow-up (<8, 8–12, >12–16, or >16)

RESULTS

Patient Demographics

- A total of 237 patients with TDT were identified in the CPRD-HES linked database and matched to 1,184 controls (**Figure 1**)

Figure 1. Patient Attrition



TDT, transfusion-dependent β-thalassemia.
[a]The number of total patients with β-thalassemia was likely overestimated due to potential misclassification; this number likely includes patients with a β-thalassemia trait; [b]Additional exclusion criteria included the following: registration within the CPRD at index, eligibility for HES data linkage, 1 year of follow-up data, and evidence of hereditary persistence of fetal hemoglobin, α-thalassemia, sickle cell disease, or hematopoietic stem cell transplant at any time in the patients' medical records.

- The mean age of patients with TDT was 24.84 years (SD: 18.92; range: 1–88), and 52.3% of patients were female (**Table 1**)
- Demographics between patients with TDT and matched controls were broadly similar (**Table 1**)

HCRU

- Patients with TDT experienced a mean rate of 17.41 inpatient hospital visits, 16.69 outpatient visits, and 24.09 outpatient prescriptions (all PPPY) (**Table 2**)
  - Of the 17.41 inpatient hospital visits PPPY, 16.62 occurred for <1 day and 0.79 occurred for ⩾1 day
- Patients with TDT had significantly higher HCRU than matched controls (**Table 2**)
- Patients with TDT received a mean of 13.62 RBCTs PPPY (SD: 4.11) during follow-up

Table 1. Baseline Demographics

	Patients With TDT (N = 237)[a]	Matched Controls (N = 1,184)[a]
Age (years), mean (SD; range)	24.84 (18.92; 1–88)	24.81 (19.16; 0–90)
Age categories (years), n (%)		
<18	93 (39.2)	466 (39.4)
⩾18	144 (60.8)	718 (60.6)
Sex, n (%)		
Female	124 (52.3)	619 (52.3)
Male	113 (47.7)	565 (47.7)
Ethnicity, n (%)		
South Asian	127 (53.6)	635 (53.6)
White	64 (27)	319 (26.9)
Other	36 (15.2)	180 (15.2)
Black	–	–
Mixed	–	–
Socio-economic status (IMD), n (%)[b]		
Q1 (lower IMD score)	23 (9.7)	146 (12.3)
Q2	34 (14.4)	174 (14.7)
Q3	47 (19.8)	242 (20.4)
Q4	71 (30.0)	285 (24.1)
Q5 (higher IMD score)	62 (26.2)	337 (28.5)

IMD, Index of Multiple Deprivation; Q, quintile; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.
[a]In all reporting, patient numbers <5 were masked (i.e., reported as "–") to protect patient confidentiality, and secondary masking was applied where required to avoid back-calculation; [b]IMD is a composite measure of material deprivation such as income, employment, education and skills, health, housing, crime, access to services, and living environment. Lower IMD score equates to less deprived; higher IMD score equates to more deprived.

Table 2. HCRU

HCRU, Mean Rate PPPY (SD)	Patients With TDT (N = 237)	Matched Controls (N = 1,184)
Hospital visits (any)*	34.78 (13.92)	1.94 (3.50)
Accident and emergency*	0.67 (1.02)	0.39 (0.90)
Inpatient*	17.41 (7.71)	0.24 (0.85)
<1 day*	16.62 (7.51)	0.14 (0.65)
⩾1 day*	0.79 (1.81)	0.10 (0.37)
Outpatient*	16.69 (10.66)	1.31 (2.63)
Primary care visits*[,b]	6.98	4.19
General practitioner*	3.99 (5.48)	2.96 (3.80)
Nurse*	2.99 (8.14)	1.23 (2.07)
Outpatient prescriptions*	24.09 (58.67)	8.61 (26.62)

HCRU, healthcare resource utilization; PPPY, per patient per year; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.
*[a]Statistical testing not conducted for primary care visits; *SD not available.*
[b]P<0.05 between patients with TDT and matched controls (Z-test).

Subgroup Analysis: HCRU

- The rate of HCRU PPPY was higher for patients with TDT aged ⩾18 years than for those aged <18 years (**Table 3**)
  - The mean rate of prescriptions PPPY showed the most marked difference (aged <18 years: 10.15 vs aged ⩾18 years: 33.10)
- Patients with TDT with a higher number of RBCTs PPPY in the follow-up period had higher HCRU than those with a lower number of RBCTs PPPY in the follow-up period (**Table 3**)
  - The mean rate of inpatient hospital visits that lasted <1 day (PPPY) showed the most marked differences

Table 3. HCRU by Subgroup

HCRU, Mean Rate PPPY (SD)	Age Subgroups		RBCT Subgroups			
	<18 Years (n = 93)	⩾18 Years (n = 144)	<8 RBCTs (n = 14)	8–12 RBCTs (n = 37)	>12–16 RBCTs (n = 131)	>16 RBCTs (n = 55)
Hospital visits (any)	31.89 (9.87)	36.65 (15.75)	20.01 (9.88)	31.16 (11.93)	34.73 (13.47)	41.09 (13.62)
Accident and emergency	0.48 (0.66)	0.80 (1.18)	1.45 (2.24)	0.67 (0.84)	0.57 (0.83)	0.73 (0.99)
Inpatient	14.99 (4.90)	18.98 (8.74)	6.77 (3.38)	14.49 (4.76)	16.54 (5.78)	24.16 (8.83)
<1 day	14.38 (4.70)	18.07 (8.58)	5.66 (3.09)	13.22 (3.90)	15.99 (5.61)	23.19 (8.64)
⩾1 day	0.61 (0.89)	0.91 (2.21)	1.12 (1.61)	1.27 (2.42)	0.55 (1.08)	0.98 (2.58)
Outpatient	16.42 (8.35)	16.87 (11.94)	11.78 (6.54)	16.00 (9.60)	17.62 (11.41)	16.20 (10.13)
Primary care visits*	4.33	8.68	19.23	7.52	6.14	5.47
General practitioner	2.56 (3.14)	4.90 (6.41)	9.44 (14.76)	4.63 (4.49)	3.23 (3.33)	3.95 (5.41)
Nurse	1.77 (3.32)	3.78 (10.04)	9.79 (21.10)	2.89 (6.74)	2.91 (7.48)	1.52 (1.84)
Outpatient prescriptions	10.15 (12.44)	33.10 (73.30)	53.54 (89.35)	29.41 (100.12)	19.39 (31.49)	24.23 (61.25)

HCRU, healthcare resource utilization; PPPY, per patient per year; RBCT, red blood cell transfusion; SD, standard deviation; TDT, transfusion-dependent β-thalassemia.
[a]SD not available.

LIMITATIONS

- This study used ICD-10 codes (HES) and Medcodes (CPRD) to identify patients with β-thalassemia and thus is subject to misclassification bias due to inaccurate coding
  - The number of patients with β-thalassemia was likely overestimated due to patients with a β-thalassemia trait being coded as having β-thalassemia
  - There is no validated algorithm for the diagnosis of β-thalassemia using CPRD-HES, and the positive predictive values for ICD-10 codes are unknown; however, the specificity of TDT is likely to be high, as it requires an additional set of criteria (⩾8 RBCTs per year for 2 consecutive years)
  - HCRU was likely underestimated because any drugs prescribed in secondary care (i.e., hydroxycarbamide, iron chelation therapies, etc.) could not be identified through the HES database
- Given the minimum 12-month post-index period for patients with TDT, individuals who died or were not continuously enrolled for ⩾12 months post-index were excluded, which could have led to an underestimation of HCRU

CONCLUSIONS

- Patients with TDT had significantly higher HCRU than matched controls from the general population in England
- Older age and a higher number of RBCTs in the follow-up period were associated with higher HCRU
- Elevated HCRU in patients with TDT highlights the need for innovative therapies that can reduce RBCT use and the associated HCRU

ACKNOWLEDGMENTS

The study was supported by Vertex Pharmaceuticals Incorporated. Editorial coordination and support were provided by Nathan Blow, PhD, under the guidance of the authors. Editorial support was provided by Iona Linford, MEng, and Nicholas Strange of Complete HealthVizion, Inc., IPG Health Medical Communications, Inc., Chicago, IL, USA, funded by Vertex Pharmaceuticals Incorporated.

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AUTHOR DISCLOSURES

This study was based in part on data from the Clinical Practice Research Datalink obtained under license from the UK Medicines and Healthcare products Regulatory Agency. The data were provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the authors alone. This study was sponsored by Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics. CU, SC, JH, and NL are employees of Vertex Pharmaceuticals Incorporated and may hold stock or stock options in the company. NFL, FCI, and SF are employees of IQVIA and may hold stock or stock options in the company. FS has received research grants from IQVIA, Novartis Pharma AG, and Vertex Pharmaceuticals Incorporated; received honoraria from Biologix FZ co, Bristol Myers Squibb, Chiesi Ltd, and Novartis Pharma AG; served as an advisory board or committee member for Agios, bluebird bio, Bristol Myers Squibb, Silence Therapeutics Plc, and Vertex Pharmaceuticals Incorporated; and acted as Chair for the UK Forum on Haemoglobin Disorders.

Presented at The Professional Society for Health Economics and Outcomes Research (ISPOR) Annual Scientific Meeting, May 7–10, 2023, Boston, MA, USA