Routine management, healthcare resource use and patient/caregiver-reported outcomes of patients with transfusion-dependent β-thalassaemia in the United Kingdom: a mixed methods observational study

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PosterCast

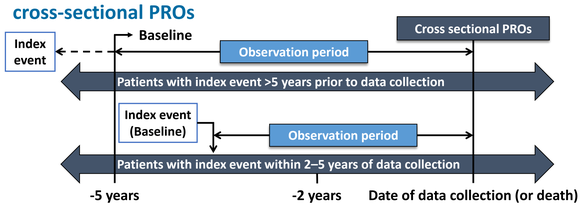
INTRODUCTION

- β-thalassaemia is an inherited blood disorder that results in defects in haemoglobin (Hb) synthesis.[1]
- The most severe forms of β-thalassaemia require regular blood transfusion therapy to sustain life (transfusion-dependent β-thalassaemia [TDT]).[2]
- Long-term blood transfusion therapy causes iron overload; regular monitoring of iron burden and iron chelation are essential to reduce the risk of complications.

STUDY DESIGN

- A multicentre, observational study was conducted in 9 NHS secondary care centers in the UK; the study involved retrospective data collection and cross-sectional patient reported outcome (PRO) questionnaires (completed at enrolment by patient/caregivers). The study design is shown in **Figure 1**.
- The observation period was defined as the five year period prior to the date of data collection/death **or**; for patients with a diagnosis of TDT between two to five years prior to the date of data collection/death, the observation period was from the date of diagnosis of TDT to the date of data collection.
- Baseline was defined as the start of the patient's observation period.
- The index event was defined as the date on which the decision to commence long-term blood transfusion therapy was documented in the patient's medical record *or* the date of the first transfusion within the first 12 month period where at least 8 transfusions for β-thalassaemia were recorded.

Figure 1. Study design; retrospective chart review with cross-sectional PROs



METHODS

Study participants

- Inclusion criteria:
  - Patients with a documented diagnosis of TDT ≥2 years prior to data collection. This study defined transfusion dependence as treatment with ≥8 transfusions during the first year of chronic transfusion therapy or a history of at least 100 mL/kg/year of packed red blood cells.
- Exclusion criteria:
  - Patients who had undergone allogeneic haematopoietic stem cell transplant (allo-HSCT), except those who had disease recurrence post-transplant who were receiving transfusion therapy and met the definition of TDT
  - Living patients for whom written informed consent had not been obtained.

METHODS CONTINUED

- Exclusion criteria (continued):
  - Patients with <2 years of continuous data available prior to data collection.
  - Patients participating in any clinical trial during the study observation period.
- Inclusion criteria for parents/carers:
  - Parents/carers aged 16 years or older.
  - Parents/carers who self-identify as a primary carer for a patient who has consented to participate in the cross-sectional survey.
- Exclusion criteria for completion of PROs only:
  - Patients or caregivers with any significant mental or English language incapacity that would have prevented them from participating.

Data sources

- Data were collected retrospectively from consenting patients' medical records, including demographics, clinical characteristics, TDT treatment, monitoring and iron chelator therapy.
- Validated PRO questionnaires were completed by eligible patients/caregivers at enrolment. PROs included:
  - EQ-5D-3L[3] (or EQ-5D-Y for patients aged 8–15)
  - TranQoL[4] (thalassaemia-specific Quality of Life [QoL])
  - Work Productivity and Activity Impairment (WPAI-SHP)[5]

Statistics

- Distributions and descriptive statistics of central tendency (mean or median) and dispersion (standard deviation [SD] or interquartile range [IQR]) were calculated for quantitative variables. Nominal variables were described with frequencies and percentages.

RESULTS

- 165 study patients were included in the study (1 patient was deceased at data collection). 134 patients completed ≥1 PRO questionnaire(s); 37 caregivers completed ≥1 questionnaire(s).

Baseline characteristics

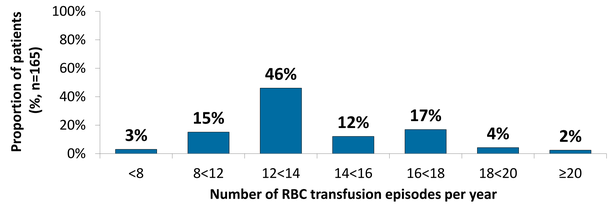
- The median age at the end of the observation period was 24.1 [interquartile range (IQR) 11.8–37.2] years; 50% (n=82) were male and one patient was deceased.
- The median age at diagnosis of TDT was 1.0 (IQR 0.5–8.0) years
- The median disease duration was 11.6 (IQR 6.4–21.7) years.
- Of 156 patients with comorbidities recorded at baseline, 69% had ≥1 comorbidity.
- The most commonly recorded comorbidities (n=156) included hypogonadotrophic hypogonadism (20% [n=31]), vitamin D deficiency (16% [n=25]) and osteoporosis (14% [n=22]); 20% (n=31) were splenectomised.

Transfusion burden

- Patients had a mean of 13.7 (SD 3.2) transfusion episodes per patient per year (**Figure 2,** the primary endpoint); 82% of patients had ≥12 transfusion episodes per year.
- Mean units of blood transfused was 32.8 (SD 10.8) per year (n=104).

RESULTS CONTINUED

Figure 2. Distribution of the number of transfusion episodes per patient per year



- Mean pre-transfusion haemoglobin (Hb, from 8473 tests) was 99.5 (SD 10.1) g/L; Patients had a mean of 17.2 (SD 5.8) Hb tests per year.

Iron burden and assessment frequency

- The recorded frequency of tests was:
  - Mean of 11.4 (SD 4.1) serum ferritin (SF) tests/year.
  - Median interval between liver iron concentration (LIC) tests was 1.9 (IQR 1.3–2.5) years.
  - Median interval between cardiac T2* was 2.5 (IQR 1.7–5.0) years.
- Median SF and magnetic resonance imaging (MRI) results (closest to the end of the observation period):
  - SF was 1961.0 (IQR 1090.0 to 3003.0) ng/ml.
  - R2 LIC (n=119) was 5.4 (IQR 2.9–11.6) mg/g.
  - T2* cardiac iron (n=132) was 30.3 (IQR 22.0–37.1) ms.
- The distributions of LIC/cardiac iron MRI test results closest to the end of the observation period are shown in **Figure 3**.

Patient and caregiver reported quality of life

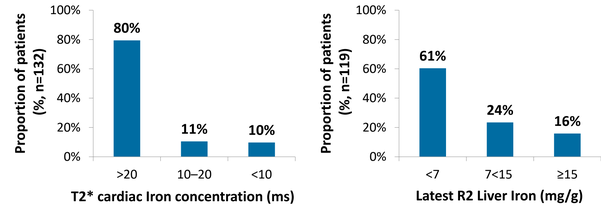
- Patient and caregiver reported outcomes are tabulated in **Table 1.**

Table 1. Results of patient/caregiver reported outcomes questionnaires

Questionnaire	Patients	Caregivers
EQ-5D-3L utility scores[a] (Reference range = -0.59–1.00)	≥16 years: 0.69 (0.33), n=94 4–7 years (proxy)[e]: 0.73 (0.27), n=9	0.88 (0.15), n=34
EQ-5D-3L VAS scores[a] (Reference range = 0–100)	≥16 years: 66.7 (20.4), n=95 8–15 years[f]: 73.0 (23.4), n=20 4–7 years (proxy)[e]: 79.2 (20.4), n=10	75.2 (16.5), n=27
WPAI (%)[b]		
Absenteeism[c]	3 (0–17)%, n=44	9 (6–25)%, n=13
Presenteeism[c]	30 (10–60)%, n=49	20 (8–43)%, n=16
Work productivity[c]	38 (23–60)%, n=44	30 (25–55)%, n=13
Activity impairment	50 (20–80)%, n=88	30 (10–50)%, n=29
TranQoL[a] (Reference range = 0–100)	≥18 years: 58.6 (18.4), n=94 7–18 years: 74.8 (15.0), n=27 <7 years (proxy)[e]: 78.1 (12.7), n=13	63.2 (21.4), n=37
TranQoL domain scores[a,d] (Reference range = 0–100)		
Physical health	54.8 (23.9), n=94	
Emotional health	58.6 (19.9), n=94	
Sexual health	65.7 (25.4), n=59	N/A
Family health	71.8 (19.8), n=94	
School and career health	51.3 (30.0), n=92	

Data presented as: [a]mean (SD), [b]median (IQR). [c]Only patients in employment. [d]Adult (≥18 years) only. [e]Completed by parent/caregiver of child in relation to the child; adult value set used to calculate index score. [f]Completed EQ-5D-Y.

Figure 3. Distribution of liver and cardiac iron concentrations



Chelation therapy

- All patients received ≥1 iron chelator during the observation period.
- At data collection 162 patients were receiving chelators.
- Median age at initiation of chelation therapy (n=91) was 2.9 (IQR 1.8–12.1) years.
- Chelators taken (at any point) included deferasirox (80% [n=132]), desferrioxamine (52% [n=85]), deferiprone (35% [n=57]) or combination therapies 21% (n=34).

SUMMARY

- These results offer insights into the real-world management of patients with transfusion-dependent β-thalassaemia (TDT) in the UK NHS, and the burden placed on patients, caregivers and healthcare resources.
- Patients appear to have been well managed; however, a subset of patients suffered severe liver (16%) or cardiac-iron (10%) loading, the latter being associated with significant mortality risk.[2]
- All patients received chelation therapy, and 21% of patients required combination chelation therapy.
- The impact of the disease on the patient/caregiver should not be underestimated as evidenced by the EQ-5D for adults utility score of 0.69 [SD 0.33] which compares with a mean value of 0.95 for UK adults (reporting no health conditions).[6]
- The WPAI results suggest that activity impairment (50%) may be comparable to or higher than reported in other chronic conditions, such as chronic obstructive pulmonary disease (13–65%) and rheumatoid arthritis (33%).[7]
- Retrospective studies are reliant on the quality of recording in the source medical records; further, as consent was required patients included in this study may not be representative of the wider patient population.
- The analysis of PROs relied on the completeness of the answers provided by participants, and answers may be subject to recall bias.

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DISCLOSURES

FS declares advisory board (silence therapeutics, Roche, Novartis), clinical safety committee (Abfero pharmaceuticals) and steering committee for trial (Celgene) involvement; PT declares advisory committee (Global Blood Therapeutics, Novartis, bluebird bio), data monitoring committee (Pfizer), clinical trial activity (Apopharma, Celgene, Global Blood Therapeutics, Novartis, Napp Pharma), investigator led funding (Kyowa Kirin Limited, bluebird bio) and speaker activity (Apopharma, Terumo plc); MV declares advisory board for bluebird bio; SP declares advisory board (Celgene, Novartis) and sponsorship to attend educational meeting (Celegene); RW states nothing to declare; SP declares Novartis support to attend educational meetings; EC declares consultancy fees from Novartis; JK declares advisory boards with Celgene, Jazz and Novartis; JH is an employee of OPEN VIE (formerly pH Associates); CP and MJ are employees of bluebird bio and own stock in the company; KR declares advisory boards for bluebird bio and Pfizer, and educational grant from Novartis.

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