Co-morbidities in Transfusion Dependent Beta(β)-thalassaemia Patients in England: A 10-Year Retrospective Cohort Analysis

Jobanputra M[1], Paramore C[2], Laird S G[3]

[1, 2] bluebird bio, Inc., Cambridge, MA; [3] insight 2 implement Ltd, Elstead, Surrey, United Kingdom

BSH18-PO-132

INTRODUCTION

Background

β-thalassaemia is a genetic disease, characterised by reduced or absent synthesis of beta-globin, ineffective erythropoiesis and haemolysis, that can lead to anaemia and other complications.[1]

Depending on severity and clinical management it is grouped into transfusion-dependent (TDT) and non-transfusion-dependent β-thalassaemia (NTDT), the former requiring frequent life-long blood transfusions for patient survival.[1]

Allogeneic stem cell transplant is potentially curative[2] but limited by donor availability and risks associated with the procedure. The majority of patients are managed with regular red blood cell transfusions and iron-chelating agents to treat chronic iron overload.

The underlying disease and its treatment are associated with a wide-range of complications, in particular, endocrinopathies, chronic hepatitis, osteoporosis and cardiovascular disease.[3]

Objective

To explore the 10-year prevalence of co-morbidities in patients with TDT using Hospital Episode Statistics (HES) data from the National Health Service (NHS) in England.

METHODS

HES is a data warehouse containing pseudonymised patient level details of admissions at NHS hospitals in England.

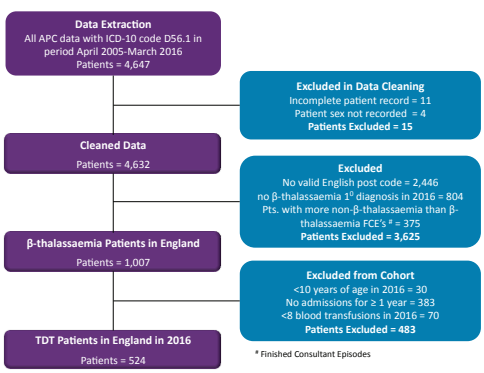
A retrospective cohort analysis was undertaken utilising HES admitted patient care (APC) data for patients with a primary diagnosis of β-thalassaemia (ICD-10 code D56.1) in the 2016 NHS year (April 2015-March 2016).

Patients with ambiguous diagnoses or not resident in England were excluded. 1,007 β-thalassaemia patients were identified, similar to the 1,032 in the National Haemoglobinopathy Registry at the time of analysis. Patients <10 years of age, without 10 years of medical records, or with NTDT (defined as receiving <8 transfusions in 2016) were then excluded. After exclusions 524 patients remained; 52% were male, median age 31.5 years, with a mean of 15.0 transfusions per patient in 2016 (median 14.0).

Ethnicity was predominantly Asian (60%); 28% of the cohort being Pakistani, 20% Indian, 5% Bangladeshi and 7% from any other Asian background.

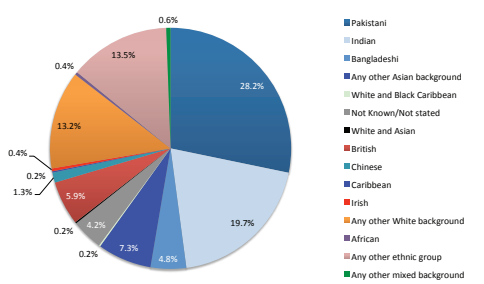
The 10-year co-morbidity prevalence rates were calculated by examining all ICD-10 diagnosis codes in cohort patients' HES APC records in the 10 years leading up to March 2016. Co-morbidities of interest were selected following a review of UKTS Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK.[4]

Figure 1: Cohort Identification



Finished Consultant Episodes

Figure 2: Ethnicity



RESULTS

Co-morbidity rates were high; 69% of patients had at least one co-morbidity of interest, while 48% had two or more and 34% three or more.

Overall co-morbidity rates increased with age; 66% of patients having a co-morbidity by age 24 and all patients developing one by 54.

Figure 3: Co-morbidity rates (all patients)

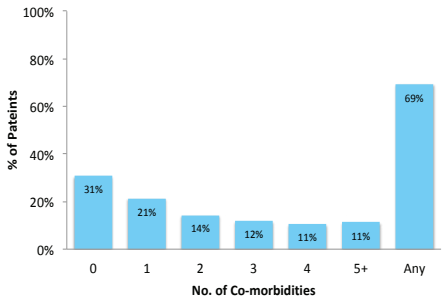
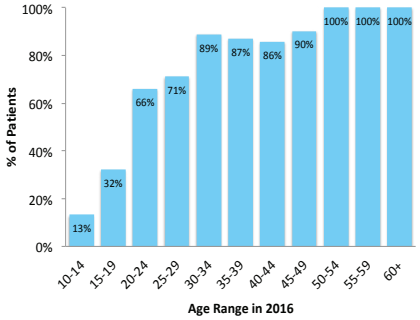


Figure 4: Patients with ≥1 co-morbidity by age range in 2016



Osteoporosis was the most common co-morbidity, affecting 45% of patients. Two other co-morbidities affected >25% of patients, hypopituitarism (33%) and diabetes (31%), with a 9% prevalence of type I and a 21% prevalence of type 2 diabetes, the remainder being classified as 'other' or 'unspecified'.

Of particular note was the high rates of co-morbidities in younger patients. In the 25-29 patient cohort there were three co-morbidities that occurred in >35% of patients (osteoporosis 44%, hypopituitarism 39% and ovarian dysfunction in 37% of female patients) and six that occurred in >25% of patients. Rates continued to increase with age, with approximately a third of patients having testicular dysfunction (males), ovarian dysfunction (females) or hypothyroidism before the age of 40. Rates of osteoporosis, hypopituitarism and diabetes were even higher in the 35-39 cohort at 59%, 51% and 46% respectively.

Table 1: 10-year co-morbidity rates (%) by age

Age Range (Years in 2016)	No. of Patients	Osteo-porosis	Hypo-pituitarism	Diabetes	Testicular Dysfunction*	Ovarian Dysfunction**	Hypo-thyroidism	Cardiac Disease	Hypo-parathyroidism	Hepatitis C†	Hearing Loss
10-14	60	0.0	3.3	3.3	0.0	0.0	1.7	0.0	0.0	0.0	5.0
15-19	65	10.8	13.8	1.5	7.3	0.0	1.5	4.6	0.0	7.7	0.0
20-24	59	35.6	27.1	15.3	20.0	16.7	15.3	6.8	6.8	6.8	1.7
25-29	59	44.1	39.0	25.4	34.5	36.7	27.1	16.9	18.6	3.4	5.1
30-34	63	57.1	54.0	41.3	46.2	33.3	25.4	12.7	12.7	7.9	7.9
35-39	70	58.6	51.4	45.7	31.4	34.3	32.9	8.6	17.1	4.3	10.0
40-44	49	65.3	36.7	40.8	31.8	18.5	18.4	24.5	10.2	10.2	10.2
45-49	51	66.7	37.3	58.8	12.0	23.1	23.5	33.3	11.8	17.6	9.8
50-54	25	88.0	40.0	56.0	50.0	11.8	24.0	44.0	8.0	16.0	24.0
55-59	16	56.3	43.8	62.5	28.6	11.1	31.3	75.0	6.3	12.5	18.8
60+	7	85.7	0.0	71.4	0.0	0.0	28.6	42.9	0.0	14.3	14.3
TOTALS	***524***	***44.7***	***33.2***	***31.3***	***23.9***	***19.5***	***19.1***	***16.4***	***9.4***	***7.6***	***7.4***

* % of males; ** % of females. † includes B171 (acute hepatitis C) and B182 (chronic viral hepatitis C); Co-morbidity rates ≥ 25% are highlighted.

Cardiac disease affected 16% of patients; the most common conditions being atrial fibrillation, with 9% prevalence, heart failure 7%, cardiomyopathy 6%, pulmonary hypertension 2% and atrioventricular block 2%.

Table 2: 10-year rates (%) of cardiac disease by age

Age Range (Years in 2016)	No. of Patients	Cardiac Disease TOTAL	Atrial Fibrillation	Heart Failure	Cardio-myopathy	Pulmonary Hypertension	AV Block	Cardiomegaly
10-14	60	0.0	0.0	0.0	0.0	0.0	0.0	0.0
15-19	65	4.6	0.0	1.5	4.6	0.0	0.0	0.0
20-24	59	6.8	1.7	3.4	3.4	0.0	0.0	0.0
25-29	59	16.9	6.8	13.6	13.6	0.0	5.1	0.0
30-34	63	12.7	4.8	11.1	4.8	0.0	0.0	0.0
35-39	70	8.6	2.9	5.7	2.9	0.0	0.0	0.0
40-44	49	24.5	10.2	14.3	6.1	2.0	0.0	0.0
45-49	51	33.3	27.5	5.9	11.8	2.0	5.9	0.0
50-54	25	44.0	32.0	8.0	8.0	12.0	4.0	0.0
55-59	16	75.0	50.0	6.3	12.5	37.5	6.3	0.0
60+	7	42.9	14.3	42.9	0.0	14.3	0.0	0.0
TOTALS	***524***	***16.4***	***8.8***	***7.3***	***5.9***	***2.3***	***1.5***	***0.0***

Co-morbidity rates ≥ 25% are highlighted

SUMMARY

- This retrospective analysis covers the 10 year period from April 2006-March 2016 and shows a high rate of co-morbidities in patients with TDT who are managed with chronic blood transfusions and chelation, suggesting significant disease burden and highlighting the need for improved treatment options.
- Osteoporosis was the most common co-morbidity, affecting 45% of patients, with high rates observed even in young patients
- Three co-morbidities affected >25% of patients, osteoporosis, hypopituitarism and diabetes, with rates of 45%, 33% and 31% respectively
- Co-morbidity rates increased with age; 66% of patients had a co-morbidity by age 24 and 100% of patients developing one by age 54
- Cardiovascular disease affected 16% of patients overall and was one of the most common co-morbidities affecting patients ≥ 45 years of age

ACKNOWLEDGEMENTS

The HES database is Copyright © 2016, re-used with the permission of NHS Digital. All rights reserved.

Editorial assistance was provided by insight 2 implement Ltd, with analytical support provided by Beacon Consulting. Funding was provided by bluebird bio Inc.

DISCLOSURES

M Jobanputra: Employee of bluebird bio Inc with stock ownership; *C Paramore:* Employee of bluebird bio Inc with stock ownership; *S Laird:* Employee and Director of insight 2 implement Ltd. Retained by bluebird bio Inc for presentation development.

References

1. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT); 2014. 2. Baronciani D et al. Bone Marrow Transplantation. 2016; 51: 536–541. 3. Bonifazi F et al. CMRO. 2017; 33(8): 1525-1533. 4. United Kingdom Thalassaemia Society; 2016