In-Hospital Death in Transfusion-dependent Beta(β)-thalassaemia in England: A 10-Year Retrospective Cohort Analysis

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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). [1]

Patients with transfusion-dependent β-thalassaemia (TDT) require frequent and life-long transfusions for survival.[1] Chronic transfusions introduce excess iron, requiring rigorous monitoring of iron burden and life-long iron chelation therapy.

Despite improvements in iron chelation treatment and monitoring, TDT is associated with increased morbidity and mortality.

Objective

To explore in-hospital mortality patterns over time in patients with TDT in England using Health Episode Statistics (HES) data and compare these with the general population.

METHODS

HES is a data warehouse containing pseudonymised, patient level details of admissions and outpatient attendances at National Health Service (NHS) hospitals in England.

A retrospective cohort analysis was undertaken utilising HES admitted patient care (APC) and outpatient data for patients with a primary diagnosis of β-thalassaemia (ICD-10 diagnosis code D56.1) in the 2006 NHS year (April 2005–March 2006).

Data were cleaned to exclude patients with ambiguous diagnoses, confirmed or possible bone marrow transplant and those not resident in England. Patients receiving ≥8 blood transfusions in 2006 were defined as TDT patients.

Historical data (2007-2016) for cohort patients were extracted from the HES database in order to evaluate 10-year in-hospital mortality rates. The in-hospital death rate of the cohort was compared with the general population in England and Wales by calculating the probability of death in an age/sex matched general population cohort over the 2007-2016 period using Office of National Statistics death rates by age and sex. Differences between observed and expected death rates were assessed using a general z-test.

450 patients met the inclusion criteria, 52% were male and the median age was 22 years (interquartile range 11.3 – 32.0). The most commonly reported ethnicities were Pakistani (26%), Indian (17%) and "Any other White background" (16%).

Figure 1

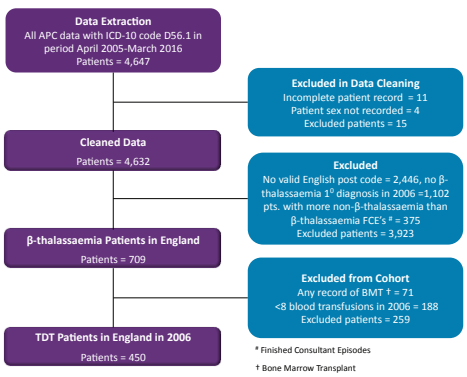
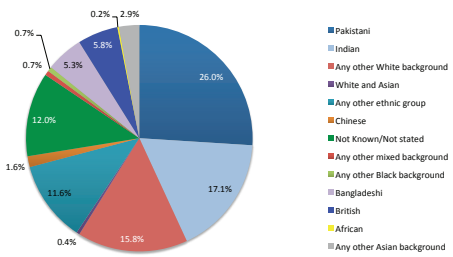


Figure 2: Ethnicity



RESULTS

Of the 450 cohort patients, 412 were known to be alive in 2016, 19 were lost to follow-up, and 19 died in hospital; the most common causes of admission at death were: liver/bile duct cancer (3), cardiac disease (3), pneumonia (2), respiratory failure (2), renal failure (2).

Median age of death was 37 years (range 8-68), with a mean age of 38.4 years. 68.4% (13/19) of deaths were in males.

Patients received a mean of 13.4 transfusions in 2006 (13.3 in 2007-2016 period). The median number was 13.0 (interquartile range 15.0 – 11.0).

Table 1: 10-year mortality by age range

Age Range (Years in 2006)	No. of Patients	TDT Cohort 10-year mortality 2007-2016			England & Wales 10-Year Mortality rate* 2007-2016 (%)
		Known Alive n (%)	Lost to Follow-up n (%)	Known Dead n (%)	
0-4	41	41 (100)	0 (0.0)	0 (0.0)^{ns}	(0.1)
5-9	52	51 (98.1)	0 (0.0)	1 (1.9)^{s}	(0.1)
10-14	54	51 (94.4)	2 (3.7)	1 (1.9)^{s}	(0.3)
15-19	56	52 (92.9)	2 (3.6)	2 (3.6)^{s}	(0.4)
20-24	54	48 (88.9)	4 (7.4)	2 (3.7)^{s}	(0.6)
25-29	58	53 (91.4)	3 (5.2)	2 (3.4)^{s}	(0.7)
30-34	45	41 (91.1)	2 (4.4)	2 (4.4)^{s}	(1.1)
35-39	46	39 (84.8)	5 (10.9)	2 (4.3)^{ns}	(1.5)
40-44	30	24 (80.0)	1 (3.3)	5 (16.7)^{s}	(2.1)
45-49	10	9 (90.0)	0 (0.0)	1 (10.0)^{ns}	(3.3)
50+	4	3 (75.0)	0 (0.0)	1 (25.0)^{ns}	(9.7)
All Patients	***450***	***412 (90.7)***	***19 (4.2)***	***19 (4.2)***^{s}	***(0.8)***

*Calculated from ONS annual death registration summary tables 2006-2016; age/sex weighted to match TDT cohort
ns= not significant; s=significant (p<0.05) vs England & Wales 10 year mortality rate.

Figure 3: 10-year mortality by age range

Figure 3 displays the % of cohort patients known to have died compared with 10-year mortality rate in England & Wales from the ONS.

A key limitation of these data is that HES is a hospital-only dataset and therefore is only able to identify those patients who died in hospital.

It may be that a number of patients lost to follow-up did in fact die in an out of hospital setting.

These data could be further refined if the HES dataset were linked to death certificate data held by the ONS.

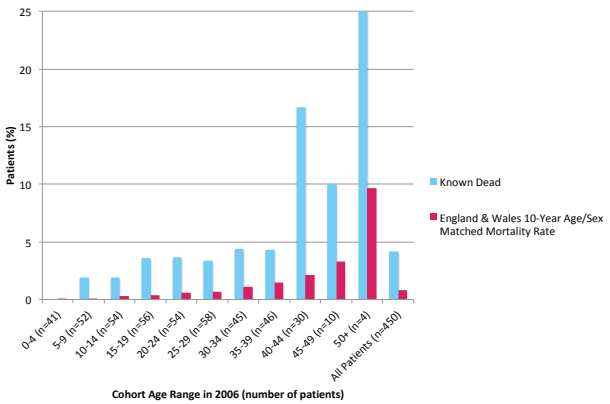


Table 2: Reason for admission prior to death in hospital

ICD-10 Chapter	ICD 10 Diagnosis Code	No. of Deaths	Ages at Death	ICD 10 Diagnosis
Blood Disorders	D561	1	28	Beta thalassaemia
Cancer	C220	2*	44, 48	Malignant neoplasm: Liver cell carcinoma
	C221	1	56	Malignant neoplasm: Intrahepatic bile duct carcinoma
	C800	1	30	Malignant neoplasm, primary site unknown, so stated
Cardiovascular	I500	1	35	Congestive heart failure
	I501	1	31	Left ventricular failure
	T827	1	52	Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts (pacemaker)
Digestive System	K550	1	19	Acute vascular disorders of intestine
	K650	1	32	Acute peritonitis
Genitourinary	N179	2	45, 68	Acute renal failure, unspecified
Infection	A419	1	50	Sepsis, unspecified
Respiratory	J181	2	29, 47	Lobar pneumonia, unspecified
	J440	1	52	Chronic obstructive pulmonary disease with acute lower respiratory infection
	J969	2	23, 27	Respiratory failure, unspecified
Unspecified	Z769	1	8	Person encountering health services in unspecified circumstances
TOTAL		***19***		

The HES database does not record cause of death. The data in table 2 records the reason for admission in the FCE in which death occurred.
* Both patients with a record of Hepatitis C infection

SUMMARY

- Patients with TDT endure a high transfusion burden, with cohort patients receiving a mean of 13.4 transfusions per annum in 2006
- The 10 year in-hospital mortality rate was 4.2% (19/450), significantly greater than the 0.8% age/sex adjusted mortality rate of the general population (p<0.0001, 95%CI: 2.54% to 6.49%)
- In the 19 patients who died, the most common cause of admission prior to death was: liver/bile duct cancer (3), cardiac disease (3), pneumonia (2), respiratory failure (2), renal failure (2)
- Despite advances in chelation treatment and iron monitoring, this analysis suggests that patients with TDT remain at increased risk of early death compared with the general population
- HES only records deaths occurring in hospital and these results are therefore likely to underestimate the overall cohort death rate, as some patients lost to follow-up may have died outside of a hospital

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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.