Iron overload in transfusion-dependent survivors of hemoglobin Bart's hydrops fetalis.

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Supplementary File

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Detail of Statistical Analysis:

- Supplementary Table 1, Univariate analysis and multiple regression of longitudinal variables
- Supplementary Table 2, Baseline variables not included in multiple regression model

Supplementary Table 1

Univariate analysis and multiple regression of longitudinal variables

Univariate analysis of potential predictors of outcomes									
	Ferritin/LIC			**Ferritin (log transformed)**			**LIC (log transformed)**		
	β	*SE*	***P-value***	*β*	*SE*	***P-value***	*β*	*SE*	***P-value***
Age at assessment [1]	5.22	4.42	**0.24**	0.01	0.02	**0.59**	-0.005	0.02	**0.80**
Disease type (α-thalassemia vs. β-thalassemia)	-213.74	33.77	**<0.0001**	-0.89	0.24	**0.0010**	0.21	0.21	**0.32**
Type of chelation medication	-112.69	38.86	**0.0050**	0.002	0.18	**0.99**	0.29	0.17	**0.09**
Method of LIC assessment	-79.03	39.19	**0.0467**	-0.09	0.15	**0.57**	0.03	0.16	**0.82**
Multiple regression of potential predictors of outcomes (excluding type of chelation medication)									
	Ferritin/LIC			**Ferritin (log transformed)**			**LIC (log transformed)**		
	β	*SE*	***P-value***	*β*	*SE*	***P-value***	*β*	*SE*	***P-value***
Age at assessment [1]	-2.16	3.39	**0.53**	-0.002	0.02	**0.91**	0.001	0.02	**0.95**
Disease type (α-thalassemia vs. β-thalassemia)	-208.97	33.19	**<0.0001**	-0.88	0.24	**0.0013**	0.21	0.22	**0.35**
Method of LIC assessment	-75.28	33.37	**0.0272**	-0.11	0.15	**0.47**	0.03	0.16	**0.87**
Multiple regression analysis with chelation type and disease type as potential predictors of outcomes									
	Ferritin/LIC			**Ferritin (log transformed)**			**LIC (log transformed)**		
	β	*SE*	***P-value***	*β*	*SE*	***P-value***	*β*	*SE*	***P-value***
Disease type (α-thalassemia vs. β-thalassemia)	-184.87	33.91	**<0.0001**	-0.88	0.25	**0.0014**	0.12	0.22	**0.59**
Type of chelation medication	-72.85	32.35	**0.0282**	0.04	0.17	**0.80**	0.27	0.18	**0.12**

Patients' gender was not included in this analysis due to limited number of patients. Method of LIC assessment was included in the model as with the change in the practice of LIC assessment from biopsy to R2-MRI in January 2004, the assessment method could have confounded the effect of age in a longitudinal data analysis and discrepancies between results of method of LIC assessment have previously been reported [Fischer R, Harmatz P, Nielsen P. Does liver biopsy overestimate liver iron concentration? Blood. 2006;108(5):1775-6; author reply 1776].

Due to the profound association between peripheral blood reticulocyte count and disease type, this variable was not included in the linear mixed model due to the risk of multicollinearity and model instability. Furthermore, the type of chelation medication was highly correlated with age and method of LIC assessment. Thus another model was constructed with type of chelation

medication and disease type as variables. Both models showed disease type was an independent predictor of ferritin-to-LIC.

1: although age at assessment was not a significant predicator of ferritin-to-LIC in the overall population, there was a reverse trend between ferritin-to-LIC with age only in homozygous α^0-thalassemia patients. As age at assessment increased, ferritin-to-LIC ratio decreased ($\rho = -0.28$, $p = 0.07$).

SE: standard error, LIC: liver iron concentration.

Supplementary Table 2

Baseline variables not included in multiple regression model.

	α -Thalassemia	β-Thalassemia	P value
Average annual serum iron [micromole/L], Mean (SD)	40.05 (5.59)	50.01 (12.51)	0.061
Average annual serum transferrin [g/L], Mean (SD)	22.26 (4.12)	20.37 (3.01)	0.24
Average annual serum iron/transferrin [micromol/g], Mean (SD)	1.79 (0.32)	2.48 (0.65)	0.021
Average annual reticulocyte count [x10e9/L], Mean (SD)	613 (82)	<20	<0.001
Ferritin at 12 months [µg/dL], Mean (SD)	1242.4 (419.4)	418.3 (113.3)	<0.001
Age of initiation of chelation [Month], Mean (SD)	16.3 (3.2)	34.2 (8.1)	<0.001
Age of chelation switch from deferoxamine to deferasirox [Year], Mean (SD)	9.8 (2.7)	9.2 (3.6)	0.73
Cardiac T2* [ms]	38.6 (3.2)	36.2 (2.5)	0.19