Serum ferritin level and morbidity risk in transfusion-independent patients with β-thalassemia intermedia: the ORIENT study

Khaled M. Musallam,[1,2] Maria Domenica Cappellini,[1] Shahina Daar,[3] Mehran Karimi,[4] Amal El-Beshlawy,[5] Giovanna Graziadei,[1] Matthew Magestro,[6] Jerome Wulff,[7] Guilhem Pietri,[7] and Ali T. Taher[2,8]

[1]University of Milan, Ca Granda Foundation IRCCS, Ospedale Maggiore Policlinico, Milan, Italy; [2]American University of Beirut Medical Center, Lebanon; [3]Sultan Qaboos University, Muscat, Oman; [4]Hematology Research Center, Shiraz University of Medical Sciences, Iran; [5]Cairo University, Egypt; [6]Novartis Pharmaceuticals Corporation, NJ, USA; [7]HERON Evidence Development Ltd., London, UK; and [8]Chronic Care Center, Hazmieh, Lebanon

Correspondence: ataher@aub.edu.lb
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Supplementary Table 1. Total hemoglobin level (g/dl) changes during the observation period (n=52).

Year	Mean	SE	95% CI		%Change from previous year	%Change from baseline
			LL	UL		
2000	9.1	0.2	8.7	9.4	0.0	0.0
2001	9.0	0.2	8.7	9.4	-0.6	-0.6
2002	9.0	0.2	8.6	9.3	-0.8	-1.4
2003	8.9	0.2	8.6	9.2	-0.9	-2.2
2004	8.8	0.2	8.5	9.2	-0.5	-2.7
2005	8.8	0.2	8.4	9.1	-0.5	-3.2
2006	8.8	0.2	8.4	9.1	-0.4	-3.5
2007	8.7	0.2	8.3	9.0	-0.8	-4.3
2008	8.7	0.2	8.3	9.1	0.0	-4.3
2009	8.6	0.2	8.2	9.1	-0.6	-4.9
2010	8.8	0.2	8.5	9.1	2.1	-2.9
				Mean	-0.3	-3.0

SE, standard error; CI, confidence interval; LL, lower limit; UL, upper limit.

Supplementary Table 2. Serum ferritin level (ng/ml) changes during the observation period (n=52).

Year	Mean	SE	95% CI		%Change from previous year	%Change from baseline
			LL	UL		
2000	513.2	51.2	410.3	616.0	0.0	0.0
2001	574.6	54.4	465.5	683.7	12.0	12.0
2002	650.7	58.3	533.6	767.7	13.2	26.8
2003	709.3	61.6	585.6	833.1	9.0	38.2
2004	765.4	68.2	628.3	902.4	7.9	49.1
2005	766.0	66.9	631.7	900.2	0.1	49.3
2006	846.0	75.3	694.9	997.1	10.5	64.9
2007	936.5	82.4	771.1	1101.8	10.7	82.5
2008	1003.6	88.8	825.4	1181.8	7.2	95.6
2009	1121.3	98.4	923.8	1318.8	11.7	118.5
2010	1209.0	103.0	1002.2	1415.8	7.8	135.6
				Mean	9.0	67.2

SE, standard error; CI, confidence interval; LL, lower limit; UL, upper limit.

Supplementary Table 3. Evaluated morbidities and their descriptions.

Morbidity	Description
Liver disease	Biopsy confirmed fibrosis, cirrhosis, or cancer
Extramedullary hematopoiesis	Radiological evidence of extramedullary hematopoietic foci with or without symptoms
Diabetes mellitus	Fasting blood sugar ≥126 mg/dl, or 2-hour post prandial blood sugar ≥200 mg/dl, or symptoms of hyperglycemia and a casual (random) plasma glucose ≥200 mg/dl[1]
Hypothyroidism	Thyroid stimulating hormone >4.7 µU/l and a free T4 <0.8 ng/dl[2]
Hypoparathyroidism	Normal or inappropriately low intact parathyroid hormone level in a patient with subnormal serum albumin corrected total or ionized calcium values, after hypomagnesemia and vitamin D deficiency have been ruled out[3]
Osteoporosis	Bone densitometry T-score -2.5 SD[4]
Hypogonadism	Secondary hypogonadotrophic hypogonadism with or without infertility or delayed puberty in females>13 years not yet Tanner B2 (i.e. prepubertal breast development) or >14 years requiring estrogen replacement therapy or >15 years with primary amenorrhea; males>14 years not yet Tanner G2 (i.e. prepubertal genital development) or an androgen replacement therapy or >17 years not yet Tanner G4 (i.e. midpubertal genital development)[5]
Thrombosis	Compression ultrasonography, contrast venography or angiography evidence of thrombus
Pulmonary hypertension	A systolic pulmonary artery pressure greater than 35 mm Hg, which corresponds to a tricuspid regurgitant velocity on Doppler echocardiography of >2.8 m/sec + exertional dyspnea without evidence of left heart disease[6]

1. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009;32(1):193-203.
2. Baskin HJ, Cobin RH, Duick DS, Gharib H, Guttler RB, Kaplan MM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002;8(6):457-69.
3. Shoback D. Clinical practice. Hypoparathyroidism. N Engl J Med. 2008;359(4):391-403.
4. El-Hajj Fuleihan G, Baddoura R, Awada H, Arabi A, Okais J. First update of the Lebanese guidelines for osteoporosis assessment and treatment. J Clin Densitom. 2008;11(3):383-96.
5. Fung EB, Harmatz PR, Lee PD, Milet M, Bellevue R, Jeng MR, et al. Increased prevalence of iron-overload associated endocrinopathy in thalassaemia versus sickle-cell disease. Br J Haematol. 2006;135(4):574-82.
6. Barst RJ, McGoon M, Torbicki A, Sitbon O, Krowka MJ, Olschewski H, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. J Am Coll Cardiol. 2004;43(12 Suppl S):40S-7S.

Supplementary Figure 1. Annual distribution of serum ferritin level categories during the observation period. SF, serum ferritin level.