ASSOCIATION OF HIGH LEVELS OF FERRITIN WITH HIGH-DENSITY LIPOPROTEIN CHOLESTEROL IN PATIENTS UNDER HEMODIALYSIS

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Background

High levels of ferritin (Fer) cause oxidative stress (OS) and inflammation. Chronic inflammation and oxidative stress are associated with metabolism of lipids such as high-density lipoprotein cholesterol (HDL-C). Reactive oxygen species (ROS) can modify the all proteins in HDL and may decrease levels of HDL-C (Blanca Murillo-Ortiz et al. Oxid Med Cell Longev. 2016;2016:1578235. Nans Florens et al. Toxins. 2016; 8: 376).

Objection

The objection of this study was to assess the association of Fer, source of iron as a generator of ROS, with HDL-C in HD patients.

Methods

1. A prospective study was designed in 267 prevalent HD patients. Exclusion criteria: patients expected to die within 6 months; malignancy, infection, acute vasculitis, liver disease and heart failure.
2. Non-fasting venous blood samples were drawn before the HD session for measuring routine biochemical parameters and albumin, lipids, adiponectin, high-sensitive CRP (hsCRP), interleukin-6 (IL-6), myeloperoxidase (MPO), oxidized low-density lipoprotein (oxidized LDL), transferrin saturation (TSAT) and Fer.
3. Nutritional state was assessed by subjective global assessment (SGA), body mass index (BMI), and normalized protein catabolic rate (nPCR).
4. Patients were followed up for 12 months and Fer, hsCRP and HDL-C were measured every three months (5 times for 12 months). Usage of erythropoiesis stimulating agents (ESA) and doses of intravenous iron were recorded.

Results

Table 1. Characteristics of patients according to ferritin quartiles at baseline

	All	Q1 (5.3, 46.6)	Q2 (47.5, 80.7)	Q3 (81.7, 131.5)	Q4 (131.8, 706.2)	p
Age (year-old)	**62 ± 13**	**58 ± 12**	**63 ± 13**	**63 ± 14**	**65 ± 11**	**0.012**
gender (male,%)	**171 (64)**	**53 (80.3)**	**45 (68.2)**	**37 (55.2)**	**33 (51.5)**	**0.002**
BMI (kg/m2)	21.5 ± 3.1	22.0 ± 3.0	21.3 ± 2.7	20.7 ± 3.3	21.9 ± 3.2	0.06
HD vintage (months)	148 (6, 489)	139 (12, 426)	129 (22, 426)	169 (18, 489)	149 (6, 189)	0.78
Primary disases(n (%))						
CGN	105 (44)	25 (43)	26 (44)	32 (51)	22 (39)	0.40
DMN	80 (34)	16 (28)	20 (34)	23 (37)	21 (37)	
BNS	29 (12)	8 (14)	7 (12)	6 (10)	8 (14)	
unknown	5 (2)	1 (2)	0 (0)	1 (2)	3 (5)	
DM (%)	33	24	33	39	36	0.31
CVD (%)	50	38	55	60	47	0.06
Kt/V	**1.5 ± 0.3**	**1.5 ± 0.2**	**1.4 ± 0.3**	**1.6 ± 0.3**	**1.5 ± 0.2**	**0.02**
nPCR (g/kg/day)	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	1.1 ± 0.2	1.0 ± 0.2	0.06
PEW (SGA positive) (%)	18	15	15	16	25	0.42
Usage of statin(%)	21	20	21	25	19	0.82
Dose of intravenous iron (mg/12months)	**717 ± 368**	**790 ± 485**	**810 ± 371**	**660 ± 265**	**601 ± 270**	**0.002**
Usage of ESA(%)	**94**	**85**	**97**	**97**	**98**	**0.006**
Hb (g/dL)	10.2 ± 1.1	10.3 ± 1.6	10.3 ± 0.8	10.1 ± 0.8	10.1 ± 1.0	0.32
Cr (mg/dL)	11.7 ± 2.7	11.8 ± 2.6	12.0 ± 3.1	11.2 ± 2.5	12.0 ± 2.7	0.31
Alb (g/dL)	**0.1 (0.1, 10.4)**	**3.9 ± 0.3**	**3.9 ± 0.4**	**3.9 ± 0.4**	**3.7 ± 0.3**	**0.02**
Hs-CRP (mg/dL)	4.16 (1.2, 78.7)	0.12 (0.05, 8.3)	0.07 (0.05, 2.57)	0.08 (0.05, 9.33)	0.12 (0.05, 10.4)	0.16
IL-6 (pg/mL)	**15.7 (3.2, 133)**	**3.9 (1.2, 25.0)**	**3.8 (1.2, 21.9)**	**3.5 (1.4, 51.1)**	**5.4 (1.2, 78.7)**	**0.045**
ADN(μg/mL)	55.4 (19.0, 436.0)	16.6±16.4	19.5±11.7	18.5±9.9	18.4±9.7	0.60
MPO (ng/mL)	77.2±30	67.4±47.7	56.6±24.5	71.6±54.8	65.7±32.6	0.21
Oxidative LDL (U/L)	0.09 (0.05, 10.4)	79,3 ± 30.1	75.4 ± 28.5	74.6 ± 30.5	80.6 ± 30.0	0.61
Serum iron (μg/dL)	53.8± 22.1	47.3±21.8	58.5±25.1	53.7±21.4	55.6±18.4	**0.03**
TIBC (μg/dL)	**272.9±62.7**	**332.4±70.0**	**275.2±43.0**	**252.0±44.2**	**231.2±39.0**	**<0.0001**
TSAT(%)	**20.9±9.5**	**15.2±7.9**	**21.7±9.8**	**21.8±9.2**	**24.4±8.3**	**<0.0001**
T-C (mg/dL)	150.0±32.0	153.5±35.0	149.0±35.1	150.8±27.1	148.6±27.9	0.80
HDL-C (mg/dL)	**45.4±14.2**	**44.8±14.3**	**49.3±15.0**	**46.4±13.2**	**41.0±13.3**	**0.009**
TG (mg/dL)	113±81	125±84	109±64	103±53	100±51	0.09

Fig 1. Changes of Fer, hsCRP and HDL-C according to Fer quantiles

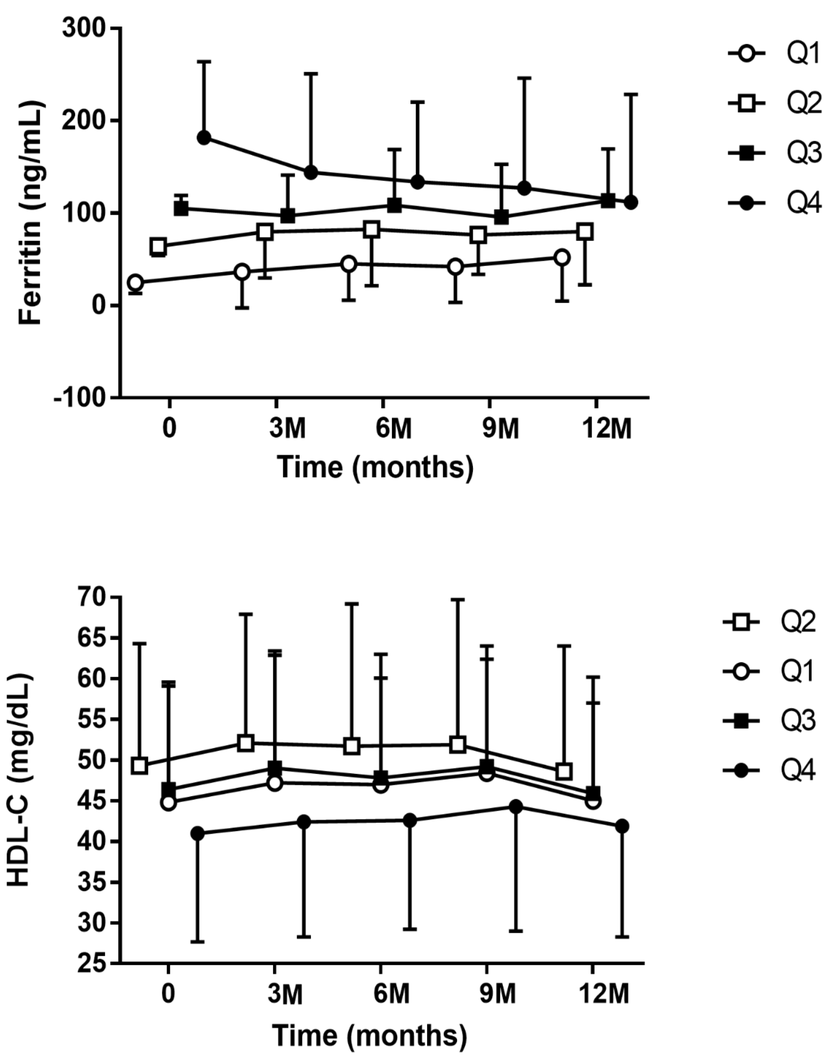

Table 2. Association between ferritin and repeated measurements of HDL-C by a multivariate approach

Quantiles of ferritin						
	Model 1		Model 2		Model 3	
	F	p	F	p	F	p
Timepoint	**13.6**	**<0.0001**	**13.1**	**<0.0001**	**12.8**	**<0.0001**
Ferritin (Q4)	**4.4**	**0.0046**	**5.2**	**0.0016**	**2.6**	**0.0497**
Interaction of ferritin and timepoint	0.45	0.9419	0.41	0.9587	0.40	0.9656
1-SD increase of ferritin						
	Model 4		Model 5		Model 6	
	F	p	F	p	F	p
Timepoint	1.3	0.2856	1.2	0.3014	1.2	0.3007
Ferritin (1SD increase)	**3.3**	**0.0108**	**2.6**	**0.0351**	**2.8**	**0.0273**
Interaction of ferritin and timepoint	0.43	0.9760	0.36	0.9902	0.41	0.9816

Model 1, 4: Repeat measurement variables for HDL-C were estimated with age, gender, diabetes mellitus status, history of CVD, SGA, albumin, BMI, TG, log hs-CRP, log IL-6, log ADN, log oxLDL, log MPO, the timepoint of each repeat measurement variable, Fer, interaction of timepoint and Fer.
Model 2: Repeat measurement variables for HDL-C were estimated with age, gender, diabetes mellitus status, history of CVD, SGA, HD vintage, BMI, nPCR, Kt/V, log AND, the timepoint of each repeat measurement variable, Fer, interaction of timepoint and Fer.
Model 5: Repeat measurement variables for HDL-C were estimated with age, gender, diabetes mellitus status, history of CVD, SGA, HD vintage, BMI, nPCR, Kt/V, log AND, log MPO, the timepoint of each repeat measurement variable, Fer, interaction of timepoint and Fer.
Model 3,6: Repeat measurement variables for HDL-C were estimated with age, gender, diabetes mellitus status, history of CVD, SGA, HD vintage, nPCR, Kt/V, BMI, TSAT, usage of statin, usage of ESA, log AND, the timepoint of each repeat measurement variable, Fer, interaction of timepoint and Fer.

Conclusion

A high Fer may be independently associated with decreasing of HDL-C levels regardless of chronic inflammation and malnutrition in HD patients.

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Disclosure of Conflict of Interest
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I have no COI with regard to our presentation.

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