FECAL CALPROTECTIN AND HB VARIABILTY : AN INTRIGUING ASPECT

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INTRDUCTION : Cronic kidney disease is a secondary cause of inflammatory syndrome . This leads to oxidative stress and arteriolosclerosis and following high incidence of cardiovascular diseases and anemia and/or ESA resistance in this setting of patients exhibiting significant within-patient hemoglobin (Hb) level variability . Recent reports focused attention on the role of bowel and microbioma as source of toxins found in high concentrations in plasma of CKD patients .

Aim of our study : to assess importance of a marker of bowel inflammation (fecal calprotectin)(FC) as a independent risk factor for Hb variability in a **setting** of hemodialysis patients undergone optimal therapy for Hb target (EBPG, NKF-DOQI), in the absence of bowel and systemic symptoms.

Tab 2 : Univariate analysis of linear with ordinal variables of Hb variability; ; * (X-bar chart) ; data are presented as mediana ;**Kruskall-wallis Z test

	Across*	High*	Low*	Target*	p**
Variation coefficient (VC)	1,2	4,67	0,11	4,34	0,03
AUC 3 months (gr/L/day)	0,72	0,43	0,52	0,17	0,07
Variation coefficient regression	0,11	0,04	0,03	0,03	0,02
Residual variance	1,31	0,56	0,4	0,41	0,007

Tab 1 : Biochemical data of hemodialysis patients stratified by Hb variability; * (X-bar chart) ; data are presented as mediana ;**Kruskall-wallis Z test

	Across*	High*	Low*	Target*	p **
Fecal calprotectin (mg/kg)	26,2	19,4	32,9	8	0,67
Age (Y)	66	78,5	68	57	0,66
PCR (mg/L)	9,46	5,1	10,1	3,45	0,35
Iron (mg/dl)	58	71	64	74	0,75
Transferrina	155	179	157	160	0,40
T sat (%)	25,5	28,2	21,9	33	0,95
Ferritin	337,1	390,8	287,2	569,9	0,84
Dialysis vintage (months)	59	48,7	61	15	0,36
Hb (gr/L)	11,75	12,7	10,7	11,73	0.005
Urea (mg / dl)	170,33	183,83	183,33	193,33	0,62
Diabetes	3/8	3/4	3/10	0/2	0,82
CVD/HBP	6/8	3/6	4/10	1/2	0,28
HCV ab	0/8	2/4	3/10	0/1	0,21

PATIENTS AND METHODS: Twenty-six prevalent hemodialysis patients clinically stable, undergone optimal therapy for Hb target, have been enrolled in a single-center study , followed for six months for time-dependent variables (Hemoglobin , urea). The choice of the follow-up period is justified as (i) 3 months provide ample time for patients to respond to ESA therapy (short period analysis (S))and (ii)allows for a retrospective analysis more comprehensive of time dependent variables (long period analysis(L)) . The fecal calprotectin was dosed in the fifth month .Baseline variables include demographic variables , binary variables (Diabetes,HCV,CVD), linear variables (Tsat,Ferritin,PCR,age, dialysis vintage). The correlation between Hb variability and fecal calprotectin is performed by two linear general models(GLM) regarding two Hb profile periods for each patient : (L)GLM (six months), (S)GLM (three months). Each model is adjusted for Urea (covariate) , and more significant variables by univariate analysis (P 0,25)

Positive interaction of fecal calprotectin (FC) with HCV

(0) HCV- ; (1) HCV+
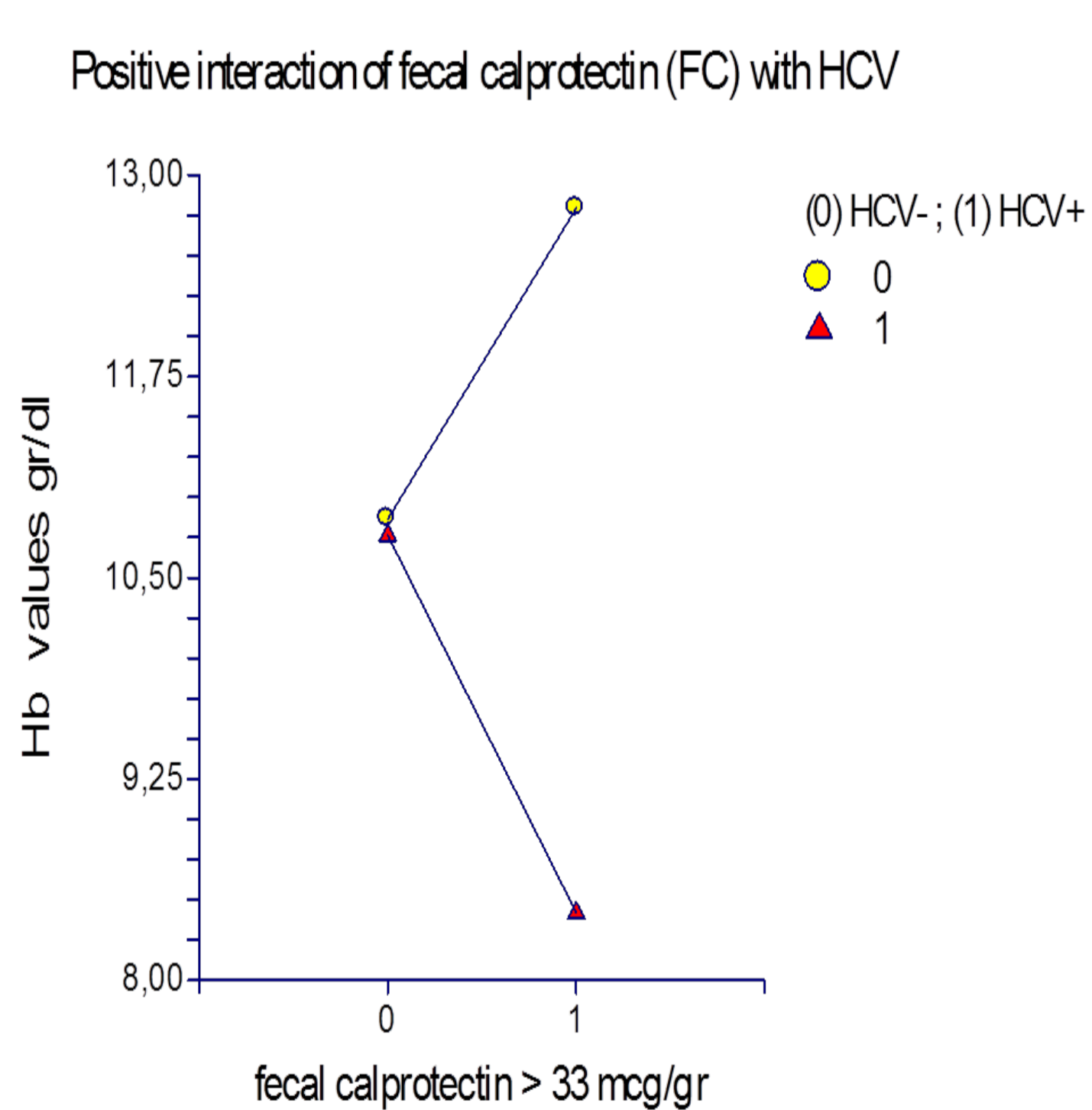
	GLM (L) 3 months				GLM (S) 6 months			
	fecal calprot		Interaction		fecal calprot		Interaction	
	F ratio	p	F ratio	P	F ratio	p	F ratio	P
Dialysis Vintage >47	6,11	0,01	4,46	0,03	5,97	0,01	0,54	0,46
T sat (%) <23	9,72	0,002	0,38	0,54	2,9	0,09	11,28	0,0001
Iron <60	8,89	0,003	5,84	0,01	4,11	0,04	5,33	0,02
RCP >7,12	3,97	0,05	1,14	0,28	4,88	0,02	0,03	0,87
Diabetes (yes)	2,08	0,15	7,04	0,009	0,00	1	0,00	1
Age >67 (y)	9,51	0,002	0,48	0,49	5,65	0,01	7,21	0,008
CVD/IPA (yes)	5,64	0,02	0,60	0,43	0,00	1	0,00	1
HCV ab (yes)	20,61	0,00002	19,38	0,00003	14,64	0,0002	0,07	0,79

Bivariate association of Hb variability with fecal calprotectin by General linear model (GLM) in two follow-up period : three months (L), six months (S)

RESULTS : FC resulted as indipendent risk factor for Hb variability in a setting of hemodialysis patients undergone optimal therapy for targeting Hb, no exhibiting bowel and systemic symptoms, both by (S)GLM analysis or (L)GLM analysis (P 0,002 and P 0,018 respectively). Data is adjusted for Urea and age . HCV ab interaction is significant both by (S)GLM analysis (P 0,00003) .

CONCLUSION : Our study demonstrate that the intestinal inflammation (such as fecal calprotectin) is an independent risk factor for variability of hemoglobin in a setting of hemodialysis patients clinically stable undergone optimal therapy for targeting Hb, regardless of age and uremic environment . This effect can be enhanced in HCV ab patients .

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