EFFECTS OF INFLAMMATION ON SERUM LEVELS OF SCLEROSTIN (SOST) IN HEMODIALYSIS (HD) PATIENTS

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INTRODUCTION AND AIMS

Produced by osteocytes, Sost inhibits Wnt pathway in osteoblasts, thus affecting bone turnover. Recently Sost levels have been reported to be increased in HD patients, with a possible negative effect on bone disease. Moreover, in experimental osteoporosis, Sost levels have been shown to positively correlate with inflammatory cytokines. Since HD patients suffer with chronic inflammation, we sought to evaluate whether inflammation affects Sost levels in HD. To our knowledge this is the first report on this topic.

METHODS

We performed a cross sectional observational study in 41 patients (59±16 y.o.) on HD since 5,9±4,8 y. None of the patient was on active vitamin D therapy. We evaluated: Sost levels and parameters of inflammation (IL1, IL6, IL10, TNFα, OPG, RANKL,) and mineral metabolism (Ca, P, PTH, 25-hydroxyvitaminD, 1,25-dydroxyvitaminD) (mean SD).
Thirty healthy subjects (34 ± 12 y.o.; eGFR 95±19 ml/min) were the control group (N).

RESULTS

Our HD population showed a moderate degree of secondary hyperparathyroidism. PTH and P were higher than N, while Ca and vitamin D lower. HD patients had a significant increment of all standard inflammatory cytokines (IL1-6-10; TNFα) and of OPG and RANKL. Sost mean levels were two-fold higher than normal. Table 1 shows mean values of the evaluated parameters.
In HD patients Sost levels correlated positively with age (r=.503; p<.001), OPG (r=.424; p<.01), IL6 (r=.419; p<.01 fig.1) and TNFα (r=.329; p<.05 fig.1) and negatively with phosphate (r=-.498 p<.001 fig.2) and PTH (r=-.347; p<.05 fig.2).

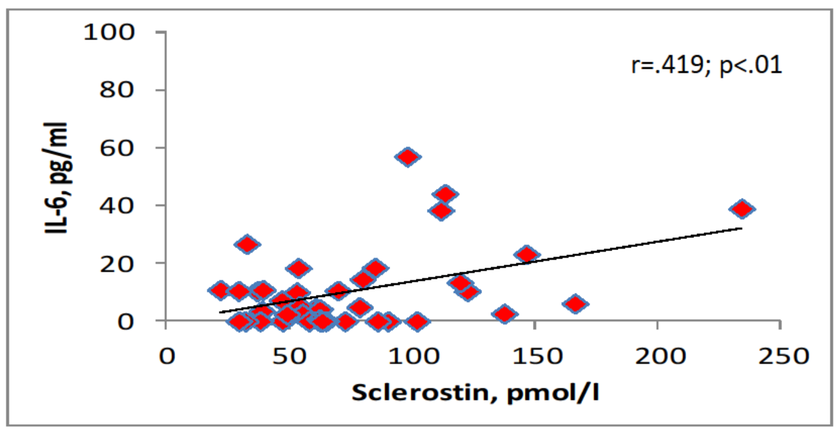
DISCUSSION AND CONCLUSIONS

Our data confirm the increment of serum Sost in HD in a range similar to what has been already reported. Importantly the negative correlations with P and PTH are in agreement with a role of Sost on bone: the higher Sost, the lower bone turnover. The positive relationship between Sost and inflammatory cytokines points to a role of inflammation on bone, exerted through Sost. Conceivably inflammation, by increasing Sost, could negatively affect bone turnover, a modulatory effect already described in HD patients.
Further, the positive correlation of Sost with age, OPG, and the inflammatory cytokines suggest also a link with artheriosclerosis. In fact, Sost levels have been recently shown to correlate with vascular calcifications in HD.
In conclusion, the increase of Sost occurring in HD could be secondary, at least in part, to inflammation.
Sost in this population can negatively affect bone turnover thus closing a circle linking inflammation and bone disease.

Table 1. Mean values of evaluated parameters

	HD	N	p<.
SOST, pmol/l	59±16	28±10	.0001
OPG, pg/ml	5±3	0,1 ±0,2	.0001
RANKL, mcg/ml	4 ± 7	0,3 ± 0,5	.0001
IL-1, pg/ml	0,27±0,58	0,01±0,01	.0001
IL-6, pg/ml	12±19	0,3±0,3	.0001
IL-10, pg/ml	9,5±11,9	4,3±1,3	.0001
TNF-alpha, pg/ml	13±11	3±2	.0001
Ca, mg/dl	8,9±0,9	9,6±0,4	.0001
P, mg/dl	4,7±1,5	3,8±0,6	.001
25D, ng/ml	11,8±6,7	18±8	.0001
1,25D, pg/ml	11,1±5,4	56±12	.0001
PTH, pg/ml	343±363	34±15	.0001

Figure 1. Correlation between Serum Sclerostin, IL-6 and TNF-alpha in HD patients.



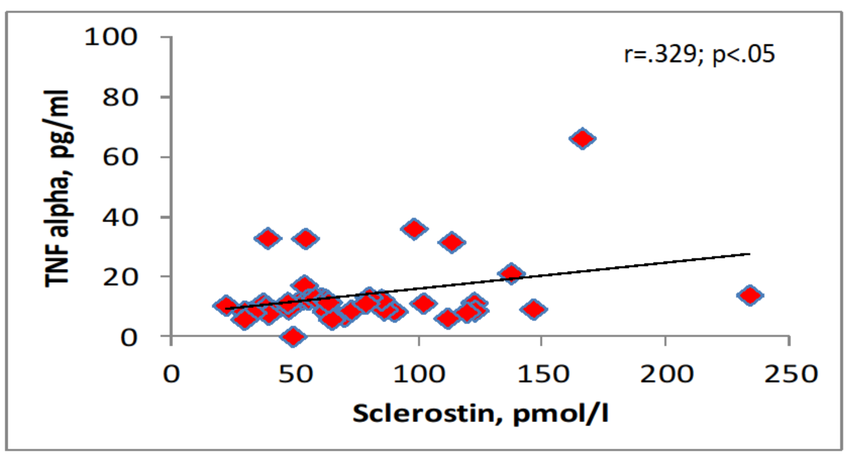
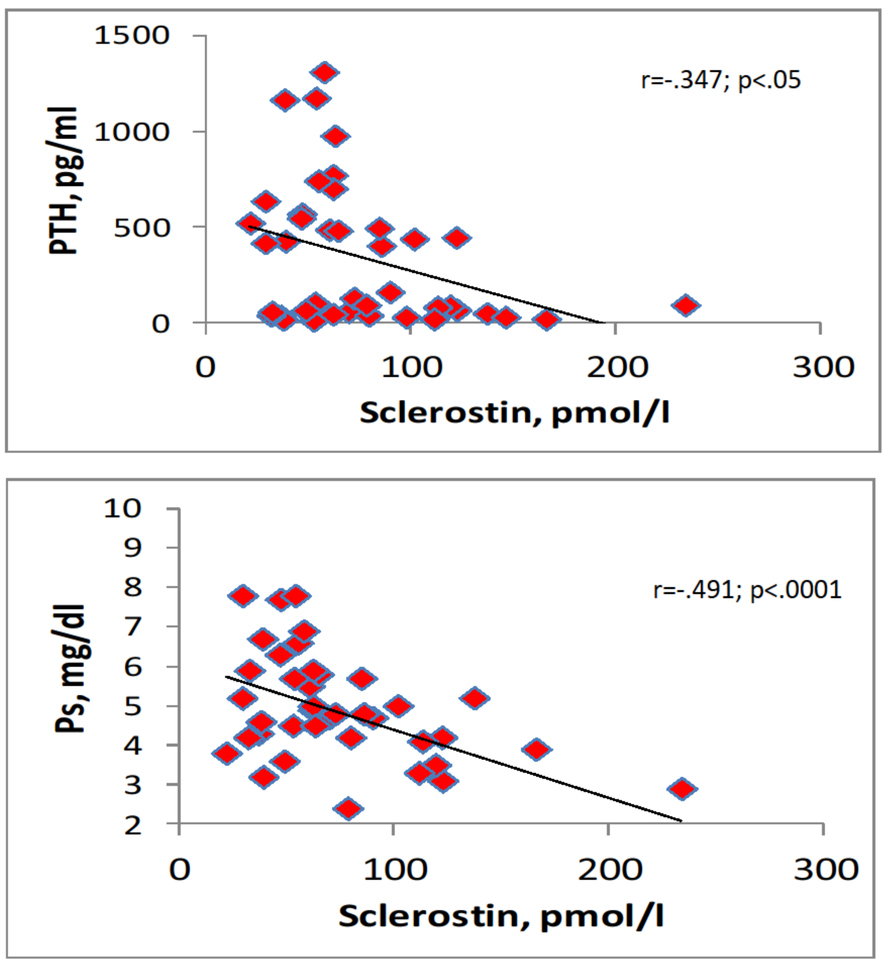


Figure 2. Correlation between Serum Sclerostin, PTH and Ps in HD patients.



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