

INTRODUCTION AND AIMS:

Vitamin D regulates bone and mineral metabolism and it plays a crucial role in maintaining adequate bone density. Recently several effects besides those on mineral metabolism has been described including cardio protector, antiproliferative and immunomodulator effects. Vitamin D deficiency is frequent in general population and in chronic kidney disease patients (Pts) including those on hemodialysis (HD). There are several studies that find a relationship between 25 OH Vitamin D (25VD) deficiency and morbidity and mortality in general population. 25VD is a stable hormone with a long half life (over two weeks) that makes it the preferable molecule to measure and assess 25VD sufficiency.

The aim of the study was to evaluate the prevalence of severe vitamin D deficiency (S25VDD) in Pts on HD and its association with mineral metabolism and hematological control and inflammatory status.

METHODS

- It's a prospective cross-sectional study
- Pts on HD for at least 3 months in dialysis at November 2013 on the center of Centro Asistencial del Sindicato Médico del Uruguay (CASMU) were included.
- The study Protocol was approved by the Ethics Institutional Committee and signed informed consent was asked to the participants.
- Data were collected from the electronic medical history regarding: age, gender, weight, body mass index, nephropathy, presence of residual renal function, erythropoietin dose (epo) / kg / week and Epo / hemoglobin (Hb) index and hospitalizations in previous 3 months.
- Midweek 25 vitamin D (25VD), PTH, ferritin, C reactive protein (CRP), Hb, calcium (Ca) and phosphorus (P) plasma levels were measured in springtime.
- Operational definitions:
 - Vitamin D levels were considered normal when ≥ 30 ng / ml, and S25VDD when < 10 ng/ml.
 - Anemia was defined by Hb < 10 g/dL
 - Slight anemia included also Pts when epo dose < 2000 UI/week was needed.
 - High Ferritin: > 500 ng/ml
 - High C Reactive Protein: > 5 mg/L.
- Pts characteristics were compared according to the presence of S25VDD.
- Risk factors for S25VDD and anemia were analyzed by logistic regression (LR)
- Comparisons were made by Chi square for categorical variables and t test for quantitative variables. Two tails P values < 0.05 were considered significant.

RESULTS I

- Were included 105 Pts (Table I) :
 - Gender: 40 females (38.1 %) and 65 men (61.9 %)
 - Age: 69.8 ± 13.2 years
 - Diabetics: 33 (31.4%),
 - Body Mass Index (BMI) 26.2 ± 5.6 kg/m²
 - Dialysis Vintage: 36.5 ± 44.9 months
- Mean 25VD level was 13.0 ± 7.5 ng/ml.
 - 107 Pts (97%) < 30 ng/ml
 - 42 Pts (40.8 %) < 10 ng/ml (S25VDD).

RESULTS II

- In univariate analysis, S25VDD was associated to increased risk of anemia (90.7% vs 75.8%) and with significant association to slight anemia (23.3 % vs 48.4 %), high ferritin (62.8 % vs 37.1 %), and high CRP (69.2 % vs 38.7 %) (Table I).
- Pts with S25VDD had higher epo resistance index (8.6 vs 5.8 UI /Kg/wk/Hb).

RESULTS III

With LR, S25VDD risk is increased by CRP level (OR: 4.59, CI95% 1.69-12.44) adjusted to gender, age, dialysis vintage, BMI, ferritin, Hb and iPTH (Table II)

With LR, S25VDD increased the risk of more than slight anemia (OR: 3.09, CI95% 1.06-9.01) adjusted to gender, age, dialysis vintage, BMI, and iPTH (Table III)

Female gender increases anemia risk (OR: 6.99, CI 1.29-38.0).

The relationship is blurred when CRO is included in the model.

Previous hospitalizations also reduce the association between S25VDD and anemia

The 27 Pts who had hospitalizations in the previous 3 months, had lower Hb (10.2 ± 1.4 vs 11.2 ± 1.4 ; $p=0.001$) and 25VD levels (10.4 ± 3.8 vs 13.8 ± 8.2 ; $p=0.004$)

CONCLUSIONS

- S25VDD is very prevalent in dialysis Pts. Its presence is associated to anemia and higher epo dose. This association could be partially explained by an increased inflammatory status (shown by high CRP and ferritin levels).
- Whether this is a causal relationship, or S25VDD is just another inflammation biomarker should be demonstrated by randomized controlled trials

TABLE I. DISTRIBUTION OF POPULATION ACCORDING SEVERE VITAMIN D DEFICIENCY

	Total	25VD<10	25VD≥10	p
N	105	43	62	
Age (x ± DS) years	69.8±13.2	71.5±11.6	69.8±14.2	NS
Femenine Gender (%)	38,1	46,5	32,3	NS
BMI (x ± DS)	26.2±5.6	26.9±6.0	25.7±5.2	NS
Diabetes (%)	31,4	39,5	25,8	NS
RRF ≥ 3 ml/min (%)	22,9	18,6	25,8	NS
HD vintage (x ± DS) months	36.5±44.9	40.9±55.4	33.5±36.1	NS
25VD (x ± DS) ng/ml	13.0±7.5	7.9±1.7	26.5±7.9	0,001
PTH (x ± DS)	449±352	486±360	424±346	NS
PTH>300 (%)	58,7	65,1	54,1	NS
Active Vitamin D Intake (%)	29,5	34,9	25,8	NS
Hb (x ± DS) g/dL	11.0±1.5	10.6±1.6	11.3±1.4	0,024
Anemia (%)	81,9	90,7	75,8	0,05
Anemia Slight (%)	38,1	23,3	48,4	0,009
EPO Use (%)	80	88,4	74,2	0,07
Resistance Index EPO/Kg/wk /Hb(x ± DS)	6.95±7.26	8.59±7.78	5.81±6.70	0,05
Epo Dose (IU/wk)	4771± 4427	5954±4938	3952±3868	< 0,05
Ferritin (x ± DS) ng/ml	511±326	592±326	455±317	< 0,05
Ferritin >500 (%)	47,6	62,8	37,1	0,01
C Reactive Protein (x ± DS) mg/dL	10.7±15.5	15.8±18.9	7.6±12.1	0,009
CRP >5 (%)	50,5	69,2	38,7	0,003
Calcium mg/dL (x ± DS)	8.90±0.59	8.85±0.60	8.94±0.58	NS
Phosphate mg/dL (x ± DS)	5.12±1.60	5.12±1.53	5.11±1.65	NS
Alcaline Phosphatase (x ± DS)	279±182	269±128	287±212	NS

TABLE II. RISK FACTORS FOR SEVERE 25VD DEFICIENCY (LOGISTIC REGRESSION)

	p	OR	Inf CI	L Sup CI
Age	0,104	1,036	0,993	1,081
Gender (reference Male)	0,129	2,172	0,798	5,907
Diabetes	0,124	0,423	0,141	1,266
PCR alta	0,003	4,59	1,694	12,44
Hemoglobin	0,094	0,734	0,511	1,054
PTHi	0,078	1,001	1	1,003
Ferritin	0,073	1,001	1	1,003
Residual Renal Function > 3ml/min	0,623	0,745	0,23	2,411
BMI	0,74	1,015	0,93	1,107

TABLE III. RISK FACTORS FOR SLIGHT ANEMIA (LOGISTIC REGRESSION)

	P	OR	Inf CI	Sup CI
Age	0,309	0,981	0,946	1,018
Gender (Female)	0,082	2,444	0,893	6,684
Diabetes	0,122	2,273	0,802	6,443
High CRP	0,662	0,802	0,298	2,158
SEVERE 25VD DEFICIENCY	0,039	3,091	1,061	9,009
PREVIOUS HOSPITALIZATION	0,004	8,225	1,969	34,356
PTHi	0,54	1	0,998	1,001
Ferritin	0,223	1,001	0,999	1,003

TABLE IV. POPULATION DISTRIBUTION ACCORDING PREVIOUS HOSPITALIZATION

	Total	YES	NO	p
N	105	27	78	
Age (x ± DS)	69.8±13.2	71.6±10.2	69.2±14.1	NS
Female Gender (%)	38,1	25,9	42,3	NS
BMI (x ± DS)	26.2±5.6	25.5±5.5	26.4±5.6	NS
Diabetes (%)	31,4	37	29,5	NS
HD vintage (x ± DS) months	36.5±44.9	53.4±67.4	30.7±32.6	0,023
25VD (x ± DS) ng/ml	13.0±7.5	10.4±3.8	13.9 ±8.2	0,036
PTH (x ± DS) ng/ml	449±352	424±415	458±329	NS
Resistance Index (IU/kg/wk/g Hb)	6.95±7.26	9.62±6.85	6.02±7.20	0,026
Hb (x ± DS)	11.0±1.5	10.2±1.4	11.3±1.4	0,001
Slight Anemia (%)	38,1	14,8	46,2	0,004
Ferritin (x ± DS) ng/ml	511±326	610±452	458±329	NS
C Reactive Protein (x ± DS) mg/L	10.7±15.5	21.1±24.0	7.5±10.0	0,001
Phosphorus (x ± DS) mg/dL	5.12±1.60	4.57±1.51	5.30±1.60	0,043