

## ASSESSMENT OF VITAMIN D DEFICIENCY AND INSUFFICIENCY IN 2 INDEPENDENT COHORTS OF PATIENTS WITH SYSTEMIC SCLEROSIS.

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**Background:** Vitamin D is a steroid hormone essential not only for bone and mineral homeostasis but also for immune response, although the vitamin D levels required to maintain optimal immune system homeostasis have not yet been established.

**Purpose:** To investigate 25-OH Vitamin D levels in two independent systemic sclerosis (SSc) populations from France and Italy and relationships with disease phenotype.

**Methods:** 160 consecutive SSc patients were included: 95 from Northern France (Paris) and 65 from Southern Italy (Cagliari). Demographic characteristics were comparable for the two groups of patients for gender, age and disease duration, only cutaneous subsets differed with more frequent diffuse cutaneous subtype in the French cohort (56% vs 18%,  $p=0.002$ ). Routine clinical assessment was performed including usual laboratory tests, Doppler echocardiography, lung CT scan, and pulmonary function tests. 25-OH vitamin D, parathormon, calcium and phosphorus were measured in all SSc patients. Vitamin D concentrations below 30 ng/ml were considered as insufficiency, while values below 10 ng/ml were classified as deficiency.

**Results:** Vitamin D insufficiency and deficiency rates were comparable between the two populations: 74/95 (78%) vs 57/65 (87%) for insufficiency and 29/95 (30%) vs 15/65 (23%) for deficiency, respectively in the French and Italian SSc patients. They were not influenced by vitamin D supplementation, which at usual dosage (800 IU/day) was not statistically different among the 2 groups (30% vs 45%,  $p=0.1$ ) and did not influence insufficiency or deficiency occurrence. The prevalence for the whole population was 131/160 (81%) for insufficiency and 44/160 (44%) for deficiency. Vitamin D deficiency was not associated with other marker that could be impaired in malabsorption syndrome such as haemoglobin, ferritinemia or albuminemia or with auto-immune markers such as anti-nuclear prevalence and levels, but a slight association was seen for positive anti-centromere antibodies ( $p=0.04$ ). A significant negative correlation was found between low vitamin D serum levels and European disease activity score ( $p=0.04$ ,  $r=-0.17$ ) and more strongly with acute phase reactants ( $p=0.004$ ,  $r=-0.23$  for erythrocyte sedimentation rate;  $p=0.01$ ,  $r=-0.22$  for C Reactive Protein values). Vitamin D deficiency was associated with systolic pulmonary arterial hypertension ( $p=0.004$ ) and pulmonary fibrosis ( $p=0.04$ ).

**Conclusion:** Vitamin D deficiency appears to be very common in these two SSc populations, independently from UV irradiation and usual vitamin D supplementation; it is associated with disease activity, pulmonary fibrosis and systolic pulmonary arterial hypertension but more strongly with inflammatory activity. Low 25-OH vitamin D serum levels in SSc may be linked to multiple risk factors: scarcely sun exposure due to disability; insufficient intake and malabsorption due to esophageal and gastric involvement; use of drugs that could alter the metabolism of vitamin D (steroids, hydroxychloroquine). Besides, our data confirm that vitamin D supplementation at standard dosage does not correct the deficiency in these patients, suggesting that, probably, higher dose of supplementation is needed, especially in patients with high inflammatory activity.