

# Letter to the Editor

## Vitamin D insufficiency is very frequent and linked to inflammatory biomarkers in relapsing polychondritis

Dear Editor,

Relapsing polychondritis (RP) is a rare autoimmune disorder characterized by chondritis of the nasal and auricular cartilages associated with tracheal/bronchi involvement. In addition, there is uveitis, hearing involvement, glomerulonephritis, and heart disease<sup>1,2</sup>. Vitamin D deficiency is associated with the presence of several autoimmune diseases<sup>3,4</sup>. Nonetheless, no study has assessed the frequency of hypovitaminosis D in RP. This study aimed to evaluate the frequency of vitamin D deficiency and insufficiency in sera from patients with RP and correlate them to the disease's possible laboratory manifestations.

This study included 22 RP patients who fulfilled McAdam's criteria<sup>5</sup>. The clinical, demographic, and laboratory data were collected from the patient charts. The exclusion criteria used were supplementation with calcium and vitamin D, immobilization during the last six months, renal failure, intestinal malabsorption problems, and bisphosphonate use. 25-hydroxyvitamin D (25OHD) levels were measured by an electrochemiluminescence assay (Elecsys Vitamin D total II, Roche Diagnostics, Swiss) with a coefficient of variation < 5.5%. 25OHD values  $\leq$  of 30 ng/ml were indicative of insufficiency, and equal to or less than 10 ng/mL were considered deficiency<sup>3</sup>. C-reactive protein (CRP) was measured by nephelometry and erythrocyte sedimentation rate (ESR) by the modified Westergren method. JASP statistical program was used. Results are expressed as mean  $\pm$  standard deviations, median (range), or percentages, and Spearman's or Pearson's correlation was also calculated. Significant results were set as  $p < 0.05$ .

The mean age of all RP patients was  $43.9 \pm 9.9$  years; 91% were female, and 73% were Caucasian. The average disease duration was  $5.2 \pm 4.0$  years. The mean weight was  $81.2 \pm 19.9$  kg, and height was  $1.66 \pm 0.08$  meters. All patients received or were under systemic glucocorticoid. Comorbidities were seen in all but one patient and included obesity ( $n=7$ ), diabetes mellitus ( $n=4$ ), and systemic hypertension ( $n=3$ ). ESR median values were 25 mm/1<sup>st</sup> hour (range: 2-140 mm/1<sup>st</sup> hour), and CRP had a median value of 7.675 mg/dL (0.1-65.9 mg/dL). The mean value of 25OHD among all patients was  $19.7 \pm 6.2$  ng/mL. Importantly, the frequency of 25OHD insufficiency was 91% and deficiency 18.2% (Table I). Interestingly, a negative correlation was observed between vitamin D and ESR ( $\rho = -0.595$ ,  $p = 0.003$ ) and vitamin D and CRP ( $\rho = -0.606$ ,  $p = 0.002$ ). No significant correlation was observed between vitamin D and age ( $r = 0.010$ ,  $p = 0.963$ ), vitamin D and weight ( $r = 0.034$ ,  $p = 0.875$ ).

The present study demonstrated that all RP patients had vitamin D insufficiency. This frequency is very high in comparison to healthy young adults (36%)<sup>5</sup>, and also, in other studies<sup>6,7</sup> that showed that 42 to 65% of the Brazilian population have low 25OHD levels. Furthermore, this study had a significant advantage in including only patients with exclusive RP, excluding those with other rheumatologic autoimmune diseases.

Possible explanations for the frequent vitamin D insufficiency observed in RP include low solar exposition, obesity, and the autoimmune itself. Besides the fact that several autoimmune diseases, such as SLE and many other autoimmune conditions, may present vitamin D deficiency<sup>8</sup>, it is conceivable to believe in the existence of autoantibodies against vitamin D, which may

**Table I.** Data from RP patients and their laboratory features.

Data	Results
Mean age, years	43.9 ± 9.9
Female gender, %	91%
Disease duration, years	5.2 ± 4.0
Median ESR values (range)	25 (2-140) mm/1 <sup>st</sup> hour
Median CRP values (range)	7.675 (0.1-65.9) mg/dL
Mean 25OHD values	19.7 ± 6.2 ng/mL
25OHD insufficiency, %	91%
25OHD deficiency, %	18.2%

25OHD: vitamin D; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

be implicated with its serum levels to be reduced<sup>9,10</sup>. No association with age or weight was herein verified. Although, vitamin D was negatively associated with CRP and ESR values, confirming an inflammatory process in RP and this vitamin.

We have some limitations in this study: first, the relatively small number of participants. Although, for a sporadic disease, it is usually the sample size of the studies on RP. Indeed, the present results will need to be confirmed in more extensive studies; second, we did not evaluate the seasons when vitamin D was measured, and it is well known the influence of climate on this hormone. For more explanations of vitamin D's potential role and mechanism in immunomodulation and autoimmune diseases, see references 11 to 13<sup>11-13</sup>.

In summary, the present study demonstrated, for the first time, a very high frequency of vitamin D insufficiency in patients with RP. Furthermore, vitamin D was inversely correlated with inflammatory markers measured by CRP and ESR. However, future studies are needed to confirm the present results and evaluate the vitamin D supplementation role in this disease.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### References

- 1) Haslag-Minoff J, Regunath H. Relapsing Polychondritis. *N Engl J Med* 2018; 378: 1715.
- 2) de Carvalho JF, Behrmann Martins LC, Cardoso AF, Shoenfeld Y. Relapsing polychondritis associated with heart block. *Eur Rev Med Pharmacol Sci* 2021; 25: 2050-2055.
- 3) Pelajo CF, Lopez-Benitez JM, Miller LC. Vitamin D and autoimmune rheumatologic disorders. *Autoimmun Rev* 2010; 9: 507-510.
- 4) Bizzaro G, Shoenfeld Y. Vitamin D: a panacea for autoimmune diseases? *Can J Physiol Pharmacol* 2015; 93: 395-397.
- 5) McAdam LP, O'Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. *Medicine (Baltimore)* 1976; 55: 193-215.
- 6) Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc* 2006; 81: 353-373.
- 7) Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, Ragi-Eis S, Chandler J. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. *J Intern Med* 2006; 260: 245-254.
- 8) Kuchuk NO, Schoor NM, Pluijm SM, Chines A, Lips P. Vitamin D status, parathyroid function, bone turnover, and BMD in postmenopausal women with osteoporosis: global perspective. *J Bone Miner Res* 2009; 24: 693-701.

- 9) Orbach H, Zandman-Goddard G, Amital H, Barak V, Szekanecz Z, Szucs G, Danko K, Nagy E, Csepany T, Carvalho JF, Doria A, Shoenfeld Y. Novel biomarkers in autoimmune diseases. *Ann N Y Acad Sci* 2007; 1109: 385-400.
- 10) Carvalho JF, Blank M, Kiss E, Tarr T, Amital H, Shoenfeld Y. Anti-vitamin D, vitamin D in SLE preliminary results. *Ann N Y Acad Sci* 2007; 1109: 550-557.
- 11) Fabbri A, Infante M, Ricordi C. Editorial - Vitamin D status: a key modulator of innate immunity and natural defense from acute viral respiratory infections. *Eur Rev Med Pharmacol Sci*. 2020; 24: 4048-4052.
- 12) Cadario F, Savastio S, Ricotti R, Rizzo AM, Carrera D, Maiuri L, Ricordi C. Administration of vitamin D and high dose of omega 3 to sustain remission of type 1 diabetes. *Eur Rev Med Pharmacol Sci* 2018 ; 22: 512-515.
- 13) Cadario F, Savastio S, Rizzo AM, Carrera D, Bona G, Ricordi C. Can Type 1 diabetes progression be halted? Possible role of high dose vitamin D and omega 3 fatty acids. *Eur Rev Med Pharmacol Sci* 2017; 21: 1604-1609.

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