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## Impact of atrophic gastritis on vitamin B<sub>12</sub> biomarkers and bone mineral density in older adults from the TUDA study

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Atrophic gastritis is common among older adults and can lead to vitamin B12 depletion owing to the suppression of gastric acid, which is required for  $B_{12}$  absorption from foods<sup>(1,2)</sup>. Emerging evidence supports a role for vitamin  $B_{12}$  in bone health<sup>(3)</sup>, but no previous study has investigated this association in relation to atrophic gastritis. This study aimed to examine the relationship of vitamin  $B_{12}$ with bone mineral density (BMD), osteoporosis risk and bone turnover markers (BTM) in older adults with atrophic gastritis. We hypothesized that atrophic gastritis has a detrimental effect on vitamin B12 status and, in turn, is negatively associated with BMD. Eligible participants (n = 2620) not using  $B_{12}$  supplements were identified from the Trinity-Ulster and Department of Agriculture

(TUDA) cohort, a study of community-dwelling adults  $\geq 60$  years recruited across Northern Ireland and the Republic of Ireland (2008–2012). Ethical approval was granted from relevant ethics committees in Northern Ireland (ORECNI; reference 08/NI/ RO3113) and the Republic of Ireland. BMD was measured via dual energy X-ray absorptiometry (DXA) at three sites: femoral neck, total hip and lumbar spine (L1–L4). Atrophic gastritis was identified via ELISA using a pepsinogen I:II ratio <3. Vitamin B<sub>12</sub> biomarkers (serum total B12; serum holotranscobalamin; plasma homocysteine) and BTM were measured.

Atrophic gastritis was associated with lower  $B_{12}$  status (all three biomarkers; P < 0.001) and a higher prevalence of deficiency (combined  $B_{12}$  index; 37% vs 17%; P < 0.001). The risk of osteoporosis (T-score < -2.5) was examined by binary logistic regression. Age (OR = 1.05, 95% CI 1.02 - 1.07 P < 0.001), female sex (OR = 2.03, 95% CI 1.44 - 2.88 P < 0.001), BMI

(OR = 0.84, 95% CI 0.81-0.87 P < 0.001), physical inactivity (OR = 1.62, 95% CI 1.07-2.44 P 0.021), previous fracture (OR = 1.49, 95% CI 1.12–1.97 P = 0.006) and bisphosphonate use (OR = 2.26, 95% CI 1.63–3.13 P < 0.001) were significant risk factors for osteoporosis. In participants with compared to without atrophic gastritis, after adjustment for BMI and 25- hydroxyvitamin D concentrations, BMD [mean (95% CI) g/cm2] was lower at the total hip [0.944 (0.920, 0.968) vs 0.974 (0.967, 0.982); P = 0.038] and lumbar spine [1.096 (1.063, 1.129) vs 1.134 (1.124, 1.145); P = 0.025], but not significantly so at the femoral neck [P = 0.089]; and the prevalence of osteopenia/osteoporosis was higher (69% vs 61%; P = 0.054). In addition, mean (95% CI) concentrations of the bone resorption marker, tartrate-resistant acid phosphatase [TRAP; 3.3 (3.1, 3.5) $\mu$ g/ml vs 3.0 (3.0, 3.1) $\mu$ g/ml; P = 0.002], was significantly higher in those with atrophic gastritis.

In conclusion, atrophic gastritis lowers vitamin B12 status and is associated with lower BMD and a greater risk of osteoporosis in older adults. Further research is warranted to investigate the relationship of atrophic gastritis and related vitamin  $B_{12}$  status with bone health in ageing.

## References

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