**Associations of major depressive disorder and related clinical characteristics with 25-hydroxyvitamin D levels in middle-aged adults**

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Background: Vitamin D deficiency has been suggested to contribute to the onset of depression, but published results are inconsistent. The aims of this study were 1) to compare serum 25-hydroxyvitamin D (25(OH)D) levels in patients with depression and non-depressed controls and 2) to examine whether distinct subtypes and symptom severity of depression may vary in their association with 25(OH)D. Methods: The study involved cross-sectional data of n=1169 participants from the BiDirect Study (n=639 patients with clinically diagnosed major depressive disorder (MDD), n=530 controls). Serum 25(OH)D was measured via LS-MS/MS. We performed analysis of covariance to evaluate adjusted means of 25(OH)D levels and multinomial logistic regression to assess the association of depression and its clinical characteristics, namely distinct subtypes and symptom severity, with 25(OH)D status (adjusted for age, sex, education, season of blood sample collection, and lifestyle factors). Results: In total, 45.0% of the participants had adequate 25(OH)D levels (≥20 ng/ml), whereas 24.9% had a deficiency (<12 ng/ml). Patients with MDD had lower 25(OH)D levels than controls (16.7 vs. 19.6 ng/ml, p<0.001). Patients with atypical depression had the lowest levels (14.6 ng/ml). Symptom severity was inversely related to 25(OH)D. Moreover, patients with MDD had a more than 2-times higher odds of 25(OH)D deficiency than controls. Atypical depression showed the highest odds of deficiency. Conclusions: The results support that patients with depression have lower 25(OH)D concentrations than non-depressed individuals. Distinct subtypes, particularly the atypical subtype, may play a special role in this context. Therefore, depression heterogeneity should be considered in future research.

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