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Letter to the Editor

The potential significance of vitamin D binding protein polymorphism in COVID-19

With interest, we read the paper by Nasiri al. (Nasiri et al., 2021), which investigated the relationship between vitamin D and the prognosis in Coronavirus Disease 2019 (COVID-19) patients. A significant association between the hospital stay and lower serum vitamin D levels was demonstrated. Although several confounders were taken into account, we would like to focus on the potential important influence of vitamin D binding protein (DBP) polymorphisms on the reported results.

DBP is a polymorphic protein with three major phenotypes, DBP1F [rs7041-T (ASP), rs4588-C (Thr)], DBP1S [rs7041-G (ASP), rs4588-C (Thr)], and DBP2 [rs7041-T (ASP), rs4588-A (Lys)], and more than 120 variants. The majority (85-90%) of 25-hydroxyvitamin D in the circulation is bound to DBP, whereas 10-15% is loosely bound to albumin, and < 1% circulates in its free form (Speeckaert et al., 2014). As demonstrated in a cross-sectional study, plasma concentrations of DBP, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D are highest in DBP1-1, intermediate in DBP2-1, and lowest in DBP2-2. Multiple regression analysis showed that the DBP concentration was an independent predictor of 1,25-dihydroxyvitamin D, whereas the DBP phenotype was a significant predictor of the 25-hydroxyvitamin D concentration, even after adjustment for confounders (Lauridsen et al., 2005). Besides rs7041 and rs4588, a genome-wide meta-analysis identified additional SNPs that affect the 25-hydroxyvitamin D concentration: e.g. rs2282679 of the *DBP* gene, which is a near-perfect proxy for rs4588. rs2282679-A is typically co-inherited with rs4588-C, whereas rs2282679-C is co-inherited with rs4588-A. rs2282679-C/C allele carriers have lower vitamin D concentrations than carriers of one rs2282679-C-allele, who in turn on average have lower vitamin D levels than rs2282679-A/A individuals (Wang et al., 2010).

Investigating the influence of the DBP phenotypes in patients with a Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection, we demonstrated that DBP1 carriers might be less susceptible to infection and mortality due to COVID-19 (Speeckaert et al., 2021). Besides, in a recent paper, a positive correlation was observed between the Metabolism score (= DBP rs2282679 + CYP24A1 rs17216707) and COVID-19 disease severity, in which a deeper analysis showed that the rs2282679 polymorphism could explain most of this interesting correlation (Freitas et al., 2021). Besides the transport of vitamin D and its metabolites, DBP could exert several other key roles in COVID-19, being involved in the extracellular actin scavenger system or acting as a neutrophil chemotactic factor and a macrophage activator (Delanghe et al., 2015).

Conflicts of interest

None disclosed.

Ethical Approval

N/A.

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