CYP2R1 GENETIC POLYMORPHISMS ARE ASSOCIATED WITH LOWER 25-HYDROXY VITAMIN D LEVELS IN LEBANESE SUBJECTS

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Introduction: Despite plentiful sunshine in the Middle East, populations in general, and in Lebanon in particular, have some of the lowest levels of 25-hydroxy vitamin D (25-OHD) worldwide. Our group has demonstrated such findings across the lifespan; predictors include gender, season, and clothing style [http://staff.aub.edu.lb/~webcmop/publications.html]. However, the possibility of an underlying genetic modulation of circulating 25-OHD levels remains unexplored. 25-hydroxylation is mainly driven by cytochrome P450 2R1 (CYP2R1) drug metabolizing enzyme; we therefore hypothesized that carriage of CYP2R1 single nucleotide polymorphisms (SNPs) may be associated with variability in 25-OHD levels.

Patients (or Materials) and Methods: Baseline 25-OHD levels were obtained for 172 Lebanese elderly patients, 60% females, age: 70.9 ± 4.3 (mean ±SD) years; BMI: 30.3 ± 4.8 Kg/m²; with vitamin D, 25-OHD: 18.7 ±7.9 ng/ml. Genotyping was performed for 4 functionally important SNPs (rs12794714, rs10741657, rs1562902 and rs10766197) in CYP2R1 gene using Real-Time PCR. Means were first compared with univariate analysis, and then multivariate regression analysis was run adjusting for age, gender, BMI, and season.

Results: Minor allele frequencies were 0.50, 0.29, 0.36 and 0.49 for rs12794714, rs10741657, rs1562902 and rs10766197, respectively; proportions comparable to those reported in Caucasian populations. Univariate analysis showed that carriers of the rs12794714 and rs10766197 variant alleles are associated with baseline 25-OHD that was 3.24 ng/ml and 4.48 ng/ml lower, respectively (P=0.018 and 0.004). This significant association remained for rs10766197 after adjusting for covariates (β= -6.401, 95%CI [-11.775; -1.027], P= 0.020).

Conclusion: This is the first study that shows the association of genetic polymorphisms in CYP2R1 with hypovitaminosis D in the Middle East. Further analysis is ongoing to evaluate the effect of these SNPs on 25-OHD levels achieved after supplementation with different doses of vitamin D.

Disclosure of Interest: None Declared