Common Variants in Vitamin D Binding Protein (VDBP) Influencing Serum 25(OH)D Level in Hong Kong Infants

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**Introduction**

- Vitamin D is a steroid hormone and plays an essential role in infancy development and associated with a wide range of diseases in deficiency state.
- Apart from the known external factors such as limited sun exposure and dietary options, genes controlling vitamin D metabolic pathways was determined as a factor controlling serum 25(OH)D level.
- The pre-vitamin considered in inactive form until it went through two metabolisms with the aids from vitamin D binding protein (VDBP) which is a carrier protein.
- Rs7041 and rs4588 exonic polymorphisms and the combined haplotypes or VDBP protein isoforms were found in regulating VDBP binding affinity to 25(OH)D and serum 25(OH)D concentration.
- Objective: Identify possible risk alleles/haplotype in VDBP and establishing a genetic relationship to the risk of vitamin D deficiency in our infants.

**Methods**

- Study cohort: 302 Healthy Chinese infants and toddlers were recruited from MCHC of different districts, aged 2-24 months.
- Genotyping by allelic discrimination from the extracted leukocytic DNA samples.
- Serum 25(OH)D level was measured by LC/MS-MS, passed UK External Quality Assessment Scheme (DEQAS).

**Results**

**Fig.1** Allelic frequency of rs7041 and rs4588 and association with serum 25(OH)D in Hong Kong infants. Rs7041 alleles associated with serum 25(OH)D level with rs7041A is identified as a risk allele, but dominant in Hong Kong infants. Genotype rs7041CC showed significant higher vitamin D level than rs7041AA. RS4588 did not show any associations with the measured 25(OH)D level with similar level measured in alleles and genotypes.

**Fig.2** Gender, a potential gene-environment interacting factors on serum vitamin D level. Identified risk genotype with girl carriers are found to have significantly lower serum vitamin D levels compared with boys, suggesting potential higher risk of vitamin D insufficiency/deficiency with rs7041A infant girls.

**Discussion**

- There are 74.43% of HK children are sufficient in vitamin D, 18.36% is insufficient and 7.21% fall under deficient.
- The allele frequency of rs7041 and rs4588 follows Chinese Han and other East Asian ethnicity groups.
- The significance of rs7041 to serum 25(OH)D suggested genetic factors regulating vitamin D level in Hong Kong infants, with higher influencing activity of rs7041 than rs4588 in VDBP protein.
- Gender interacts with genetic factors with girls rs7041A carriers showed significantly lower vitamin D level than boys, indicating a vitamin D deficiency high risk groups in Hong Kong infants.
- The data can be used as a basis for screening for high-risk infants to have early interventions diminishing the possibilities in pathogenic development of the associated diseases.