Genetic Marker Polymorphisms in The VDR and MTHFR Genes Among osteoporotic and normal Palestinian Women

Author(s):
Riham Smoom
Hisham Darwish

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Abstract:
Osteoporosis is a complex skeletal disease, characterized by low bone mineral density (BMD) and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility, leading to higher susceptibility to fractures. Many recent studies indicated that BMD is – at least in part – genetically determined. However, the most common candidate genes appearing to be closely linked with variation in BMD and high risk to develop osteoporosis, are vitamin D receptor (VDR) and methylene tetrahydrofolate reductase (MTHFR) genes. The hypothesis that commonly occurring polymorphisms in the VDR and MTHFR genes affect BMD has raised great interest. Several studies have confirmed this relationship– although some are contradictory –, while others showed negative findings.

In the present study, we analyzed the Bsm-I , Fok-I , Apa-I, and Taq-I polymorphisms in the VDR gene, in addition to the (C677T) polymorphism in the MTHFR gene, using RFLP-PCR, and investigated their correlation with BMD at the hip, the lumbar spine, and the femoral neck regions, in 344 postmenopausal Palestinian women with mean age of 61 years (67 ± 18 years) from Bethlehem district. Secondly, we also analyzed whether this correlation is associated by allelic interaction of the indicated polymorphic sites and other related factors including years after menopause, height, weight , multivitamins or calcium daily supplements intake.

The results clearly indicate the presence of significant associations between the B-allele of the Bsm-I and the t-allele of the Taq-I VDR polymorphisms with low BMD. Significant correlation between the CT genotype in the MTHFR gene and lower BMD at the spine was also indicated. However, our results showed that the Fok-I & Apa-I VDR polymorphism alone are weak predictors of BMD. Interestingly, the results of the various VDR allelic interactions indicate significant associations. Moreover, the correlation between the MTHFR and VDR polymorphic genotypes and BMD at the three indicated sites showed strong interaction. The association between the allelic variation and the other related non-genetic factors indicate the presence of significant correlation between them in predicting the BMD level.