

TLR4 Gene Polymorphism and Biochemical Markers as a Tool to Identify Risk of Osteoporosis in Women from Karachi

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Abstract : Background: Osteoporosis, characterized by low bone mineral density, poses a global health concern. Diagnosis increases the likelihood of developing osteoporosis, a multifactorial disorder marked by low bone mass, elevating the risk of fractures in the lumbar spine, femoral neck, hip, vertebrae, and distal forearm, particularly in postmenopausal women due to bone loss influenced by various pathophysiological factors. Objectives: The aim is to investigate the association of serum cytokine, bone turnover marker, bone mineral density and TLR4 gene polymorphism in pre and post-menopausal women and to find if any of these can be the potential predictor of osteoporosis in postmenopausal women. Material and methods: The study participants consisted of Group A (n=91) healthy pre-menopausal women and Group B (n=102) healthy postmenopausal women having ≥ 5 years' history of menopause. ELISA was performed for cytokine (TNF α) and bone turnover markers (carboxytelopeptides), respectively. Bone Mineral Density (BMD) was measured through a dual X-ray absorptiometry (DEXA) scan. Toll-like Receptors 4 (TLR4) gene polymorphisms (A896G; Asp299Gly) and (C1196T; Thr399Ile) were investigated by PCR and Sanger sequencing. Results: Statistical analysis reveals a positive correlation of age and BMI with T scores in the premenopausal group, whereas in post-menopausal group found a significant negative correlation between age and T-score at hip ($r = -0.352^{**}$), spine ($r = -0.306^{**}$), and femoral neck ($r = -0.344^{**}$) and a significant negative correlation of BMI with TNF- α (-0.316^{**}). No association and significant differences were observed for TLR4 genotype and allele frequencies among studied groups. However, both SNPs exhibited significant association with each other. Conclusions: This study concludes that BMI, BMD and TNF- α are the potential predictors of osteoporosis in post-menopausal women. However, CTX and TLR4 gene polymorphism did not appear as potential predictors of bone loss in this study and apparently cannot help in predicting bone loss in post-menopausal women.

Keywords : osteoporosis, post-menopausal, pre-menopausal women, genetics mutation, TLR4 gene polymorphism

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