# Association of RANK gene variants with its circulatory level and bone mineral density in postmenopausal women with and without osteoporosis

**Priya Dixit[1], Israr Ahmad[1], Shah Waliullah[2] and Tabrez Jafar[1,*]**
[1]Department of Biotechnology, Era University, Lucknow 226 003, India
[2]Department of Orthopaedic Surgery, King George Medical University, Lucknow 226 003, India

**The present study aims to explore the possible association pattern of receptor activator of nuclear factor kappa B (RANK) gene variants (rs 35211496 and rs 1805034) with its circulatory level and bone mineral density (BMD) in North Indian postmenopausal women. In this case-control study, we recruited 165 postmenopausal osteoporotic women as cases (age 54.44 ± 6.00) and 165 healthy postmenopausal women as controls (age 54.47 ± 6.46). BMDs were taken in all subjects using dual energy X-ray absorptiometry at different skeletal sites, and genotyping was carried out using polymerase chain reaction and the restriction fragment length polymorphism method. RANK serum levels were also assessed in all enrolled subjects by enzyme-linked immunosorbent assay. Findings from the present study indicated that subjects with homozygous mutant TT genotype of rs35211496 (NC_000018.10 : g.62354528C > T) and rs1805034 (NC_000018.10 : g.62360008C > T) showed significantly low BMD at forearm, lumbar spine, hip and femoral neck and increased RANK level as compared to CC and CT genotypes. Furthermore, at rs1805034, a significant difference was noted in the frequency of RANK genotypes and alleles among osteoporotic cases and controls ($P = 0.021$; 0.005) respectively.**

**Keywords:** BMD, haplotype, osteoporosis, receptor activator of nuclear factor κ B, receptor activator of nuclear factor kappa-B ligand.

menopause owing to a decrease in estrogen level, affecting calcium absorption by the kidney, intestine and bone[6]. Postmenopausal osteoporosis is a global epidemic identified by the decline of estrogen level and persistent calcium deficiency with ageing, along with the majority of women being asymptomatic unless a fracture occurs, resulting in a significant financial burden on patients, their families and the society as a whole[7,8].

The worldwide scenario of osteoporosis is that approximately 200 million women suffer from this disease, with about one-tenth of women over the age of 60, one-fifth of 70 years, two-fifths of 80 years and two-thirds of 90 years[9]. In the Indian context, 20% of the 230 million women who ages over 50 have osteoporosis[10,11].

Bone remodelling is defined as a unique process consisting of two distinct signalling equilibria: osteoblastogenesis (bone formation) and osteoclastogenesis (bone resorption). Cellular interaction of osteoblasts and osteoclasts maintains the quality and quantity of bone[12-14]. Osteoclasts are one of the essential effector cells for bone resorption. They originated from the hematopoietic cells of the monocyte-macrophage lineage and produce macrophages and dendritic cells[15-17].

RANK is the receptor of the receptor activator of nuclear factor kappa B ligand (RANKL) and is expressed as an osteoclast precursor during bone remodelling. The RANK ligand activates RANK and stimulates tumour necrosis factor (TNF) receptor-linked factors to be recruited to the RANK cytoplasmic domain, causing the induction of pathways: p38 mitogen-activated protein kinase (MAP kinase), IkB kinase (IKK), Jun N-terminal ki-