

**SERUM INSULIN-LIKE GROWTH FACTOR 1 (IGF-1),
IGFBINDING PROTEIN3 (IGFBP-3), OSTEOCALCIN, AND
URINARY FREE PYRIDINOLINE IN POSTMENOPAUSAL
OSTEOPOROSIS, AND THEIR RELATIONSHIP TO BONE
MINERAL DENSITY (BMD) BEFORE AND AFTER THERAPY.**

THESIS
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BY

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Abstract : Insulin-like growth factors (IGFs) are polypeptides synthesized under growth hormone stimulation mainly in the liver (Bala et al ;1981). They are regulatory peptide involved in many processes of cell physiology and pathology (Andreatta ;1994). IGF-I may modulate osteoblast-osteoclast interactions and serve as a coupling agent in the bone remodeling cycle (Ohlsson et al;1998). The aim of this study is to evaluate the possible alternations in the level of IGF-I and IGFBP-3 in relation to BMD in postmenopausal women and to determine if these altered levels are implicated in the pathogenesis of the disease. Also to correlate these altered levels of IGF-I and IGFBP-3 with new biomarkers of bone formation (intact osteocalcin) and bone resorption (free pyridinoline). Finally to measure the effect of treatment with different therapeutic modalities on the rate of bone turnover by biochemical markers and BMD. Two population were studied. Group 1 : consisted of twenty healthy perimenopausal women aged 33-50 years (mean age 40.5 years + 0.94; mean +SE). They had normal lumbar spine BMD, measured by dual x-ray-absorptiometry-DEXA. The second group consisted of 90 postmenopausal women (45 – 75 years) [mean 58.5+4.8 years] who all were at least five years past a natural menopause (Mean 16+ 7.2 years]. They had a lumbar spine BMD measured by DEXA more than two standard deviations below the normal mean for healthy perimenopausal women. Postmenopausal women were randomly allocated to one of five treatment groups. **Group I** (20) cases : Hormone replacement therapy in the form of Estraderm TTS 100 plus primolut N oral tablets (scHRT). **Group II** (20) cases: Oral 10mg Alendronate (Fosamax) administered orally once daily in the morning . **Group III** (20) cases: Calcitonin, Salmon nasal spray, 200 IU/day. **Group IV** (20) cases: 1,25 α hydroxyvitamin D3 (Alphacalcidol) in a dose of 0.25 μ g/day. **Group V** (10) cases: combined therapy of HRT and Bisphosphonates. All subjects also received 500mg/day elemental calcium. Serum IGF-I, IGFBP-3, osteocalcin were all determined by a two site immunoradiometric assay. Urinary pyridinium crosslinks was determined by a competitive enzyme immunoassay. This study **concluded** that growth factors (IGF-I and IGFBP-3) play an important role in the pathogenesis of postmenopausal osteoporosis. The study also shows that biochemical markers may be useful in selecting the appropriate treatment. This study also suggested that IGF-I may be a new biomarker used to monitor antiresorptive treatment.

Key Words : Insulin-like growth factor-I (IGF-I), Insulin-like growth factor binding protein-3(IGFBP-3), Osteocalcin, Pyridinolin, Osteoporosis, Bone mineral density(BMD), Biomarkers , Growth factors, Hormone replacement therapy (HRT), Calcitonin, Bisphosphonates, Alphacalcidol.