SUMMARY AND CONCLUSION

Osteoporosis is a disease that may have a tremendous impact on the lives of many postmenopausal women. Osteoporosis and its potentially devastating sequelae of fracture are increasing as the population ages and assessment of skeletal health is an important component of a women’s routine care.

More concrete efforts are needed for prevention, early diagnosis, feasible and affordable management of osteoporosis patient. We hypothesized that biochemical markers can enable dynamic and rapid measurement of total body skeletal metabolism and will be clinically useful in the management of PMO and also for assessing the effects of antiresorptive therapy. With this view, the present study was designed.

1. To evaluate the extent of osteoblastic and osteoclastic activity assessed by determining biochemical parameters in blood (serum) and urine of postmenopausal osteoporosis and non osteoporotic women.

2. Follow up study was done to evaluate the impact of specific antiresorptive therapy (alendronate + calcium + vitamin D) regimen on bone metabolism in postmenopausal osteoporosis by assaying relevant biochemical parameters, 3 months post therapy.

This study was carried out in the Department of Biochemistry, Government Medical College and Hospital Miraj and P.V.P.G Hospital Sangli. The postmenopausal women in the age group of 45 to 60 years and diagnosed as osteoporosis by clinician were selected as study group. Postmenopausal nonosteoporosis women with normal bone mineral density in the age group 45 – 60 years were selected as control subjects.
Measurement of BMD is the best quantifiable predictor of osteoporotic fracture; hence it was measured in this study. Measurement of calcium, phosphorus, magnesium was performed to provide information of the status of bone metabolism. Assay of serum albumin, vitamin C and alkaline phosphatase was done to get information about the synthesis of organic matrix and mineralization by the osteoblasts. Osteocalcin a major, valid and specific bone formation marker was assayed. TRACP activity and hydroxyproline which are specific bone resorption markers were also measured. Evaluation of results was done using suitable statistical tests.

Significant decrease in BMD scores was observed in PMO. In osteoporosis there may be exaggeration of the imbalance between bone formation and resorption. The change in activation frequency causes a transient bone loss until a new steady state between resorption and formation is achieved. The remodeling imbalance, however, results in permanent decrement in mass that can only be corrected by a remodeling event during which formation exceeds resorption. Thus significant increase in BMD scores were observed in post therapy. The antiresorptive therapy can have antiremodeling effect and may also increase intestinal absorption of calcium & phosphorus resulting in decreased bone turnover, decelerated bone loss and increasing bone strength.

BMD provides a static picture of the skeleton and thus remains the gold standard for determining the state of bone turnover and diagnosing disease.

Significant increase in osteocalcin level was found in PMO. This may be the effect of increased synthesis of osteocalcin by osteoblasts. The response to 3 months antiresorptive therapy is shown by optimization of osteocalcin level. Alendronate from this antiresorptive therapy has an indirect effect on lowering the function of osteoblast and slowly decreasing bone formation. Net positive calcium balance may be achieved during therapy. In this state osteocalcin can bind with calcium and is involved in bone calcification, hence its level may be lowered in blood circulation.
Our results clearly indicate raised osteoblastic activity in PMO, which is decreased after therapy. Thus measurement of osteocalcin can be utilized to predict the status of the osteoblastic activity during management of PMO patients.

We also found that alkaline phosphatase activity is elevated in PMO, and 3 months antiresorptive therapy normalized it. Serum alkaline phosphatase is an index marker of bone formation and its elevation demonstrates increased osteoblastic activity in PMO.

Serum calcium, phosphorus and magnesium levels were found to be significantly decreased in PMO. This might be due to low dietary intake of the principal minerals, ultimately affecting mineralization of bone. It may induce uncoupling of bone formation and resorption and may result in a loss of bone mass and high fracture rates. Significantly increase in total calcium, phosphorus and magnesium levels occurred after therapy. This might have turned off the PTH secretion and stimulated the secretion of calcitonin, a hormone that inhibits the activity of osteoclasts and thus suppresses bone resorption.

Low intake of proteins might be the cause of decreased proteins and albumin level found in PMO. Hypoalbuminemia may be the related to the reduction of bone mass. Production of IGF-I and its circulation levels might be decreased due to low protein level. Impairment of both systems may contribute to the occurrence and development of osteoporosis. All patients were advised by the clinicians to take balanced diet with adequate calcium and first class proteins. Improvement of the nutritional status might have raised the serum protein levels in post therapy.

Lowered levels of vitamin C were also observed in PMO, which may impair cross linking of protocollagen into normal collagen fibrils.

This study demonstrates that osteoblastic activity as assessed by bone formation marker is elevated in PMO and it is reduced to approach near normal levels 3 months post therapy. Osteocalcin is a promising marker of bone turnover & it can provide dynamic status of bone remodeling. Routinely
measured, simple, easy, low cost biochemical markers such as serum calcium, ALP, albumin and phosphorus could be used as indicators of increased bone turnover to enable early intervention so as to minimize fracture due to osteoporotic changes. The combined use of BMD and these biochemical markers will be of great help to the treatment decisions and to monitor effect of therapy.

The activity of serum TRACP depicted significant increase in PMO. Specific cytokines such as IL – 1, IL – 6, TNF α, GM-CSF might be responsible for this. These cytokines might have enhanced bone resorption by activation of osteoclasts. When resorption is increased in osteoporosis, TRACP secretion by osteoclasts is also increased. Significant decrease in the activity of TRACP was found after therapy. Alendronate is one of the constituent of antiresorptive therapy. It binds hydroxyapatite crystals of the bone with high affinity and inhibits bone resorption by decreasing osteoclast activity and its growth.

The present study revealed significant increase in urinary hydroxyproline in PMO.

During bone resorption, highly active osteoclasts might secrete factors such as acids, matrix metalloproteinases and cathepsin K in excess. These factors degrade more amount of collagen type I into hydroxyproline, thus increasing its excretion.

By inhibiting protein prenylation, alendronate from this antiresorptive therapy may induce apoptosis, thus reducing the number and activity of osteoclasts. This is reflected by reduced excretion of hydroxyproline post therapy observed by us in PMO.

Raised cholesterol levels found in PMO were decreased post therapy, probably due to inhibit on farnesyl pyrophosphatase.

The response of antiresorptive therapy is shown by optimization of bone resorption markers along with decreasing osteoclastic activity. Measurement of bone turnover through serum TRACP and urinary hydroxyproline could form a tool available to assist health care professionals to predict fracture risk.
Although the extent of absolute values of the individual markers varies when compared one to another, their net change after baseline can be useful to monitor therapeutic intervention and responsiveness.

In conclusion, biochemical markers of bone reflect acute changes in bone turnover rate. Bone turnover decreases in PMO women receiving antiresorptive therapy and this may be demonstrated by the decrease in the levels of marker. Alterations in the concentration of these markers can be very well utilized to monitor the effectiveness of therapy. Decrease in marker levels with antiresorptive therapy may be the early predictor of subsequent BMD increase and possible reduction in fracture risk. Therefore, bone markers should be used in combination with BMD in the management of this disease of bone metabolism.