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Commentary

Bone health status in Indian women

Osteoporosis (OP) is a major public health threat worldwide. Studies have reported that Asian women have higher predisposition for OP than their Caucasian counterparts[1]. Thus, though the exact prevalence is not known in India, one in four women older than 50 yr is believed to suffer from osteoporosis[2]. The attainment of peak bone mass in adolescent years and the rate of bone loss during postmenopausal years are some of the major factors contributing to bone health in older women[3].

The rate of bone loss accelerates during the early postmenopausal years. The accelerated bone loss in postmenopausal OP is a result of a decline in estrogen concentrations[4]. In a study on women over 40 yr of age, we found that the rate of decline in bone mineral density (BMD) ranged from 4 to 5.7 per cent from pre- to postmenopausal stage. Further, after adjusting for factors such as age, weight and height, loss in BMD of around 2.1, 2.5 and 4.5 per cent at the lumbar spine, femoral neck and total hip, respectively could be attributed to menopause[5]. BMD as measured by dual energy X-ray absorptiometry (DEXA) is believed to be a significant marker for predicting bone fragility. However, bone strength is a composite of bone density and quality, thus, there is still an uncertainty in the ability of fracture predictions based on BMD measurement alone[6]. Hence, studies, such as the one by Kumar *et al*[7] in this issue emphasize the usefulness of serum biomarkers of bone turnover (BTM) to evaluate bone health. The study also assesses the correlation between bone markers and BMD in north Indian pre- and postmenopausal women. Biomarkers (NTX and sBAP levels) evaluated in the present study[7] are negatively correlated with BMD in both femur neck and Ward's triangle, as measured by DEXA scan in postmenopausal women, similar to other studies showing an inverse correlation between sBAP and BMD[8-10].

Biochemical markers of bone remodelling, such as serum bone alkaline phosphatase (sBAP) and serum N-terminal telopeptide of type I collagen (NTX), are believed to be useful tools in the assessment of patients with metabolic bone disease[11]. As compared to imaging techniques, these have no radiation exposure, are non invasive and are also comparatively inexpensive. Another important point in the use of BTMs is their ability to measure both the formation and the degradation of bone matrix at a specific time point, hence providing information about the turnover of the tissue, rather than a static image of volume or density[12]. Markers of bone turnover can thus be used to predict the rate of bone loss in postmenopausal women; these can also be used to assess the risk of fractures[13]. Further, in osteoporosis-treatment studies (with alendronate, risedronate, raloxifene) and/or for women on hormonal replacement therapies, markers of bone turnover have been shown to be more strongly associated with fracture risk reduction than bone mineral density[14]. BTMs are also believed to be helpful in monitoring response to nutritional interventions and have the advantage over BMD in that these provide information about mechanism of effect and changes are often observed more rapidly[14].

Though biochemical markers of bone remodelling have shown promise for over the last few decades as useful tools in the assessment of patients with osteoporosis, the diagnosis of osteoporosis is still based on bone mineral density T scores as measured by DEXA scanning. By virtue of the WHO definition of osteoporosis, patients with a low bone density have increased risk of fracture[15]. However, the data indicate that bone markers predict bone loss independent of bone density; further, markers of bone resorption seem to be stronger predictors of future bone loss than markers of bone formation, and correlations are

believed to be stronger in elderly than in younger women[16]. The inherent variation of the BTMs is a limitation as these vary not only with age, gender, menopause, diseases and drugs, fractures, prolonged bed rest and immobility, but also with circadian rhythm and food[12]. These variations must thus be kept in mind when interpreting their concentrations.

Bone turnover markers, in combination with other risk factors for osteoporotic fractures, may be used to define fracture risk. In women with low bone mass, bone turnover markers are independent predictors of fracture risk. It has also been observed that vertebral fractures are directly correlated with bone turnover marker concentration and negatively with vertebral bone mineral density[15]. Fracture risk is increased if a patient has both low BMD and an increased bone turnover. Thus, in clinical practice, increased bone turnover markers in the presence of a low BMD would favour initiation of treatment for osteoporosis.

Calcium and vitamin D supplementation are the first-line strategy for the management of osteoporosis. However, several drugs including hormonal replacement therapy, selective-estrogen receptor modulators, bisphosphonates, teriparatide and strontium ranelate are other modes of therapy available for the treatment of osteoporosis[17]. While bisphosphonates, oestrogens and raloxifene decrease bone resorption and bone formation markers; strontium ranelate treatment causes a mild reduction in bone resorption markers and a mild increase in bone formation markers; teriparatide increases both bone formation and bone resorption markers. While regular yearly assessment of BMD is recommended for patients on treatment for osteoporosis, monitoring of patients on teriparatide or raloxifen may be performed by the assessment of biochemical markers of bone turnover. Some studies also suggest that patients with raised bone markers at baseline respond better to antiresorptive therapies or that stratification of patients by pre-treatment bone marker concentration may make sense from an economic point of view[15]. Reference values for bone turnover markers in adult Indian women have been described by Desai *et al*[8]. A major advantage of using bone markers is that significant changes in bone markers can be observed within three to six months after initiation of therapy allowing early intervention in those who do not show the expected response and to modulate treatment, if necessary. BMD changes on the other hand, may take 18 months to become significant; thus, it takes very long to detect treatment failure using the DEXA. In fact, fracture reduction occurs before significant changes in BMD can be established. Hence, in clinical trials, biochemical markers provide a superior signal-to-noise ratio, and therefore, these may be used to shorten duration of trials and to decrease study cohorts in size, although the variability of BTMs restricts their use at the individual level[12]. Bone turnover markers are however, invaluable in drug development and in understanding a given drug's mode of action.

Not everyone with osteoporosis has high bone turnover. However, using a holistic approach, a combination of available tools such as the WHO's FRAX risk factors assessment[18], bone turnover markers and DEXA scanning may be used for diagnosing osteoporosis, identifying "fast bone losers" and patients at high risk of fracture, selecting the best treatment and monitoring response to therapy.

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