NFI BULLETIN
Bulletin of the Nutrition Foundation of India
Volume 14 Number 4 October 1993

Osteoporotic Fractures:
An Emerging Public Health Problem in Asia?

C. Gopalan

Osteoporosis is currently a public health problem of major concern in the countries of North America and Europe. The condition clinically manifests itself in the form of fractures of the neck of the femur or compression fractures of the vertebrae. According to one estimate, by the age of 70 years, at least 40 per cent of American women will experience at least one osteoporotic fracture[1] and in 12 per cent to 20 per cent of them, the fracture and its complications would prove fatal, while in the majority of the rest prolonged supportive care would be necessary. The incidence among women is nearly double that among men.

In contrast to the above experience, osteoporosis is being generally viewed as a problem of minor public health importance in the countries of the Third World in general. For this reason, studies on osteoporosis and its clinical and public health implications have not figured prominently in the agenda of medical research in developing countries, including those of South and South-east Asia. Studies on the bone which have generally attracted attention in India are those related to the problem of fluorosis; and fluorosis had been largely looked upon (till lately) as a disease characterised by osteosclerosis rather than osteoporosis.

While it is true that on the basis of available evidence, the incidence of osteoporotic fractures is presently far less in the countries of Africa and Asia than what has been reported from the USA and Europe, there are emerging evidences to suggest that this problem may demand increasing attention in the years ahead, at least in the Asian countries. The considerations which point to such assessment are briefly the following:

- The apparently low incidence of osteoporotic fractures in populations of Asian countries, thus far, could have been partly attributable to their relatively low life expectancy. The level of peak bone mass is achieved by early adulthood and thereafter there is a progressive loss of bone density, roughly estimated to be around 1 per cent per year. It may therefore be expected that, for the reduction of bone density to reach a point that would manifest clinically as an osteoporotic fracture, a time-span of approximately 20 years may be required even in populations who start with a relatively low peak bone mass.

With increasing life expectancy, and with the sex ratio favouring the female after 40 years of age, it may be predicted that there will be a significant expansion in the po[illegible]an-didates for osteoporotic fractures in the years ahead; and these could emerge as an important h[illegible]th problem. Should this happen, the attention care of the aged could become a far more formidable problem than it would otherwise be; and there is no doubt that the proportion of the elderly among Asian populations will progressively increase in the years ahead.

- It is possible that marked growth retardation, and the consequent overall reduced skeletal mass among large sections of Asian populations, might have partially mitigated the severity of depletion in bone density attributable to low calcium intakes in childhood and adolescence.

Also diets very high in protein, of the type that usually obtain in the USA and Europe, are known to promote increased loss of calcium in the urine. Low protein diets generally in vogue in developing countries could have contributed to better calcium economy. With the progressive removal of constraints on overall growth and with improved diets and incidental increase in dietary protein intake, these 'protective' factors may not be operative in future years.

- There is convincing evidence that Africans and blacks in the USA are relatively immune to vertebral and hip fractures related to osteoporosis because of racial and genetic factors[2,3,4]. Comparative studies of changes in vertebral bone density in black girls and white girls during childhood and pu-

CONTENTS

berty show that vertebral bone density is substantially greater in black female subjects in late puberty; and that this difference eventually results in increased peak bone mass of black girls, largely accruing during the fourth and fifth Tanner stages of sexual development[5]. Bone density in black adults, both female and male, has been found to be between 10 per cent to 20 per cent greater than in white adults[4].

The metabolic factors underlying this racial difference have yet to be satisfactorily elucidated. Hormonal factors such as growth hormone, gonadotropins and sex steroid hormones, and calcium-regulating hormones like parathyroid may play a role. Asians, however, do not apparently enjoy this 'genetic' advantage which confers on black Americans relative freedom from the risk of osteoporosis.

In the development of osteoporosis, not only the level of peak bone mass that is attained in early adulthood but also the rate of subsequent bone loss — especially in the post-menopausal period — is important.

There are currently no studies on the rates and patterns of bone loss in the post-menopausal period as between American white subjects on the one hand, and American blacks and Asians on the other. It is possible that the extent and pattern of decline of estrogen levels may have an important role in determining the loss of bone mass in the post-menopausal period; and there could be genetic differences in this regard as between Asian and American women, but we have no evidences on these aspects as yet.

On the basis of such data as are presently available, it has to be concluded that Asian populations are as vulnerable and prone to osteoporotic fractures as American whites, and that if other factors contributing to osteoporosis such as longevity and sedentary lifestyles also come into play, osteoporotic fractures could emerge as an important public health problem in Asian countries.

The few research centres in the South-east Asian Region wherein technical facilities and expertise for studies on bone currently exist are now reporting a significant incidence of osteoporotic fractures (for example, Department of Medicine, Ramathibodi Hospital under Dr Rajatanavin, Bangkok, Thailand, and the National Institute of Nutrition, Hyderabad, India).

Research on this problem is currently greatly inhibited and handicapped in countries of the SEAR due to the lack of adequate sophisticated equipment. Some of the techniques that were earlier in use for assessment of bone density have now become obsolete as being not adequately sensitive. Modern techniques for determining bone density such as the one based on quantitative computer tomography (which measures only trabecular bone, metabolically more active than cortical bone, and likely to respond more rapidly to hormonal changes) and the other using dual photon absorptiometry or dual energy X-ray absorptiometry, call for expensive equipment. In addition, expertise of a high order with respect to hormonal assays and their interpretation would also be necessary for comprehensive studies on this problem.

The current paucity of data from the SEAR on this problem of emerging importance may be related to these constraints. It is, however, gratifying that at least two leading centres in the region are currently engaged in these studies. These centres must be encouraged and supported to undertake collaborative work in this area of emerging importance. Some of the issues that may need to be addressed are briefly discussed.

Possible Factors That Need Consideration

The role of calcium deficiency: The present picture regarding the epidemiology of osteoporosis would suggest a minimal role for calcium deficiency in its pathogenesis. Thus the countries wherein osteoporosis and fractures of the hip are common are precisely the countries wherein the intake of milk and dairy products in particular and the overall intake of dietary calcium in general, are high, in contrast to the low dietary calcium intake levels observed in developing countries where osteoporosis is not at present a major health problem.

Available excellent reviews of the literature on the preventive role of calcium in osteoporosis present contradictory conclusions. There are multiple factors that affect bone loss. While several factors, genetic and environmental, could possibly influence the attainment of peak bone mass, there are others which could influence the subsequent rate of bone mass growth. Osteoporosis being apparently a disease of multifactorial origin, the elucidation of the precise role of calcium deficiency in the disease is a difficult undertaking.

There is evidence supporting the view that increased dietary calcium intake can reduce the risk of osteoporosis[6,7]. It is claimed that calcium deficiency during skeletal formation could decrease peak bone mass and thereby increase the risk of fractures in later life. The skeleton reaches its maturity in late adolescence. It is estimated that 37 per cent of the total skeletal mass of adults is accumulated during the few years of adolescence. It is reasonable to argue, therefore, that adequate supply of dietary calcium in order to ensure optimal calcium balance during the active phase of adolescent growth is essential for the attainment of peak bone mass.

On the other hand, dietary calcium is apparently absorbed more efficiently during adolescence than in adulthood. Apparently while the level of dietary calcium may determine the pattern of skeletal growth and peak bone mass, it seems also possible that the momentum of growth may decide the pattern of metabolic handling of dietary calcium. The subject of dietary calcium requirement in different stages of growth and development is therefore still an unsettled issue.

The dietaries of poor Asian communities provide around 300 mg of calcium, well below the recommended levels. Asian dietaries are predominantly cereal-based; the phytin content of such dietaries may contribute to poor bio-availability of calcium. Major sources of calcium such as milk and dairy products are generally beyond the reach of the poor. Green leafy vegetables are a good source but unfortunately their intake is low. Spices such as mustard, cummin seeds, curry leaves and coriander, which often figure in Asian dietaries, are good sources of calcium[8] but they are generally taken in relatively small quantities.

Betel leaves and lime may provide some calcium, especially for the adult women who may be in the habit of chewing them[8]. Millets like *ragi*, which

are good sources of calcium, are progressively being given up[9]. On the whole, the dietary calcium intakes in Asian dietaries in all age groups including childhood and adolescence are well below recommended levels. If low dietary calcium intake is an important determinant of low peak bone mass, and of the risk of osteoporotic fractures in old age, then Asians in general must be vulnerable. The paradox, however, as was pointed out earlier, is that currently the incidence of osteoporotic fractures in these populations is less than in populations subsisting on daily diets which provide at least more than double the level of calcium contained in poor Asian diets.

Here is obviously an area which calls for intensive research.

Adolescent growth: The Nutrition Foundation of India had undertaken a multicentric study on the pattern of growth of adolescent girls drawn from the most affluent sections of the Indian population[10]. The study showed that the growth performance of the Indian girls conformed to the 50th percentile of the NCHS standard till the 12th year; thereafter (that is, between the 12th and 18th year) increments in heights of Indian girls were significantly less than those of American girls as represented by the NCHS standard. All the difference between the adult heights of American girls on the one hand, and (affluent) Indian girls on the other, accrued almost entirely during adolescence (12 to 18 years).

The authors of the study had argued that while the level of dietary calcium intake in the predominantly cereal-based Indian diets was perhaps adequate to sustain optimal growth during childhood, it was not so during adolescence, when the demand for calcium for skeletal growth is much higher (since nearly 40 per cent of the overall skeletal growth is compressed within a short time-span of just six years). The growth pattern of Indian girls during adolescence was nearly similar to that reported for Japanese girls.

If reduced dietary calcium intake results in reduced overall skeletal mass, then the effect of low calcium intake on bone density may be minimal. The 'wisdom of the body' may dictate that only such skeletal growth as is commensurate with the available dietary calcium is permitted so as to maintain 'bone quality' (adaptation). This might explain the poorer growth performance of Indian and Japanese girls during their adolescence as compared to American girls. It could be argued that growth retardation might have served to offset the possible deleterious effect of low dietary calcium intake with respect to risk of osteoporotic fractures.

The Nutrition Foundation of India had launched a study to determine the effect of calcium supplementation on the growth performance of Indian girls during their adolescence. The results of this study, which is nearing completion, may throw some significant light on this issue.

In a three-year, double blind, placebo-controlled trial of the effect of calcium supplementation (1,000 mg of calcium citrate malate per day) on bone mineral density in 70 pairs of identical twins, it was found that in pre-pubertal children whose average dietary intake of calcium approximated the recommended dietary allowance, calcium supplementation enhanced the rate of increase in bone mineral density[11]. This effect was, however, not observed in post-pubertal subjects. It was concluded from this study that calcium supplementation, especially during the period of pre-pubertal adolescent growth, would contribute to enhanced peak bone mass and it was conjectured that this would contribute towards decreased risk of osteoporotic fracture in later years.

In the post-menopausal period, the evidence for a preventive role of calcium supplementation on bone mass appears to be even less convincing[12,13,14,15]. Maintenance of bone mass during pre-menopausal years seems to be primarily dependent on the integrity of ovarian function rather than on level of dietary calcium. On the whole, estrogen deficiency rather than dietary calcium deficiency seems to emerge as the major cause of post-menopausal osteoporosis.

However, most of the studies on the effect of calcium supplementation have been carried out on populations on adequate levels of calcium intake. The effect of such supplementation in populations as in Asia subsisting on substantially lower levels of calcium could be different. This is an area which would call for painstaking rigorously controlled epidemiological studies of fairly long duration with laboratory and technical support of an extremely high order.

Indian Studies On Osteoporotic Fractures

Veena Shatrugana *et al*[16] had carried out a retrospective study of osteoporotic fractures at the National Institute of Nutrition in Hyderabad, India. They came up with the remarkable finding that the general impression that osteoporotic fractures were rare in India may not be justified.

The records of cases admitted to a single hospital in Hyderabad during a 10-month period (January to October 1987) which they analysed showed that there were as many as 396 cases of fractures. While fractures in female subjects under 40 years of age were mostly work/accident related, those in subjects above 40 years of age were mostly osteoporotic fractures. Indeed, practically all fractures in subjects above 60 years of age were osteoporotic fractures. There were as many as 176 cases of osteoporotic fractures in women above 40 years of age in their sample (Tables 1 and 2). The authors indicate that this number could be an underestimate for the reason that quite a few records could not be traced. Their data would show that osteoporotic fractures in women over 40 years of age in the southern part of India are by no means uncommon.

These data raise some important and interesting issues which would call for further research. Evidence for such high incidence of fractures of the hip is not available from hospitals in other parts of the country. It is noteworthy that compression fractures of the vertebrae do not figure in Veena Shatrugana

Table 1: Distribution of Sample

Age in years	Women	Men
Under 40	80 (27.7 %)	61 (57 %)
40 and above	209 (72.3 %)	46 (43 %)
Total	289	107

Source: Reference 16

Table 2
Types of Fractures in Women over the Age of 40

Kind of fracture	Number	Per cent
Osteoporotic		
Neck of femur	145	69.3
Shaft of humerus	18	8.6
Radius (Colle's)	8	3.8
Pelvis	5	2.4
Other fractures	33	15.9
Total	209	100

Source: Reference 16

et al's sample. We will return to this point later in this paper.

Fluorosis: Unlike perhaps in the USA and Europe, an important factor that has to be taken into account in the interpretation of data on osteoporosis and osteoporotic fractures in India, and possibly in some other countries of Asia, is the problem of fluorosis. As in India, in parts of China and the Arusha region of Tanzania and South Africa also, diets that are low in calcium and a high fluoride intake produce a metabolic bone disease, characterised by osteosclerosis in some parts of the skeleton and osteoporosis and possibly also osteomalacia, in other parts.

A syndrome of endemic genu velgum in fluorosis endemic areas characterised by osteoporosis, osteomalacia and osteosclerosis had been described in adolescent and young adults in India[17]. There have been attempts to treat type I osteoporotic vertebral fractures through fluoride administration[18]; a history of femoral neck fractures is a specific contradiction for such treatments. Increased incidence of hip fractures in osteoporotic patients following on fluoride therapy have been reported [19,20], though there appears to be some controversy over this subject as on the significance of the painful 'lower extremity syndrome' which develops as a side effect of fluoride therapy.

Fluorides apparently have the property of inducing osteosclerosis preferentially in the vertebral bones, and in the presence of low calcium diets this is associated with depletion of minerals from limb bones leading to their osteoporosis.

It may be important to review Veena Shatrugana *et al*'s interesting data in the light of these considerations. It is noteworthy that their sample included several subjects who were just over 40 years of age — not really in the extreme 'geriatric' category. Secondly, and more importantly, while fractures of the neck of the femur predominated in their series of cases, vertebral fractures were virtually absent. It is possible that there were vertebral fractures in the series, but in the absence of specific investigations directed to this, possibly they were missed.

Hyderabad is not exactly a fluorosis-endemic area but the possibility of the major hospital there having attracted patients from nearby fluorosis-endemic areas cannot be ruled out. Increased fluoride retentions in subjects subsisting on sorghum (*jowar*) diets, as compared to those on rice-based diets, has been reported[21]; and *jowar* does figure prominently as a staple in the diets of some poor income groups in the area.

What we may thus be dealing with there is not the geriatric osteoporotic fractures of the USA and Europe but a syndrome of osteoporotic fractures of the neck of the femur incidental to fluorosis in which high fluoride intake, low calcium dietaries and post-menopausal loss of bone density (in the case of women past 40 years of age) may all be contributing factors. Studies currently in progress at the National Institute of Nutrition by Veena Shatrugana *et al* may throw light on this interesting possibility.

— — —

The foregoing account will show that studies on osteoporosis in the context of generally low dietary calcium intake (and high fluoride content in water in some pockets), must find a place in the future nutrition research agenda of South-east Asian countries. Such studies will not only present interesting academic challenges but could also be of practical value. They may throw light on the unsettled issue of optimal dietary calcium requirement, possibly contribute towards the prevention of osteoporotic fractures in the elderly, and towards the better management of the problems of the aged.

References

1. Nilas, Lisbeth: Calcium intake and osteoporosis. In: Simpoulos, A.P., Galli, C. (eds) Osteoporosis: Nutritional aspects. *World Rev Nutr Diet*, 73:1-26, 1993.

2. Cummings, S.R., Kelsey, J.L., Nevitt, N.C., and O'Dowd, K.J.: Epidemiology of osteoporosis and osteoporotic fractures. *Epidemiol Rev*, 7:178-208, 1985.

3. Melton, L.J., and Riggs, B.L.: Epidemiology of age-related fractures. In: Avioli, L.V. (ed) The osteoporotic syndrome: Detection, prevention and treatment. 2nd ed, Orlando, Fla, Grune & Stratton, pp 1-30, 1987.

4. Pollitzer, W.S., and Anderson, J.J.: Ethnic and genetic differences in bone mass. A review with a hereditary vs environmental perspective. *Am J Clin Nutr*, 50:1244-1259, 1989. [Erratum, *Am J Clin Nutr*, 52:181, 1990].

5. Gilsanz, V., Roe, T.F., Mora, S., Costin, G., and Goodman, W.G.: Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med*, 325(23):1597-1600, 1991.

6. Matkovic, V., Kostial, K., Simonovic, I., *et al*: Bone status and fracture rates in two regions of Yugoslavia. *Am J Clin Nutr*, 32:540-549, 1979.

7. Holbrook, T.L., Barrett-Connor, E., and Wingard, D.L.: Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet ii*:1046-1049, 1988.

8. Gopalan, C., Rama Sastri, B.V., and Balasubramanian, S.C.: Nutritive value of Indian foods. (Revised and edited by Narasinga Rao, B.S., Deosthale, Y.G., and Pant, K.C.) National Institute of Nutrition, Hyderabad, 1991.

9. Narasinga Rao, B.S.: *Nutrition News 8*, No 5, National Institute of Nutrition, Hyderabad, 1987.

10. Growth of affluent Indian girls during adolescence. *Scientific Report No 10*, Nutrition Foundation of India, 1989.

11. Johnston, C.C., Miller, J.Z., Slemenda, C.W., Reister, K.T., Siu Hui, M.S., Christian, J.C., and Peacock, M.: Calcium supplementation and increases in bone mineral density in children. *N Engl J Med*, 327:82-7, 1992.

12. Horsman, A. and Gallagher, J.C., Simpson, M., *et al*: Prospective trial of estrogen and calcium in post-menopausal women. *Br Med J ii*:789-792, 1977.

13. Recker, R.R., Saville, P.D., and Heaney, R.P.: Effect of estrogens and calcium carbonate on bone loss in post-menopausal women. *Ann Intern Med*, 87:649-655, 1977.

14. Recker, R.R., and Heaney, R.P.: The effect of milk supplements on calcium metabolism, bone metabolism and calcium balance. *Am J Clin Nutr*, 41:254-263, 1985.

15. Nordin, B.E.C., and Polley, K.J.: Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal post-menopausal women. *Calcif Tissue Int 41* (suppl 1):IS-59S, 1987.

16. Shatrugana, V., Soundarajan, N., Sundaraiah, P., and Raman, L.: Back-pain, the feminine affliction. *Economic and Political Weekly*, April 28, pp 2-6. 1990.

17. Krishnamachari, K.A.V.R., and Krishnaswamy, K.: *Lancet*, 2:877, 1973.

18. Boivin, G., Dupuis, J., and Meunier, P.J.: Fluoride and osteoporosis. In: Simpoulos, A.P. and Galli, C.,