Summary
1) Environmental factors, Ca, vit-D, exposure to sunlight and weight bearing exercises are more important than genetic in achievement of Peak Bone Mass (PBM). 2) Regular weight bearing exercise during adolescence and in young adulthood is a more important factor than Ca intake for acquisition of PBM. 3) A maximal bone mass at skeletal maturity is the best protection against osteoporosis, bone loss and subsequent fracture risk. 4) Regular mechanical, head loading or gravity resistant exercise is the single most important factor that can even offset the metabolic consequences of dietary Ca deficiency and estrogen deficiency. 5) Lifetime Ca intake and physical activity exert highly significant positive effect on bone mass, its preservation, stabilization and in preventing postmenopausal bone loss. 6) Regular adequate Ca intake and exercise can effectively offset the adverse effects of estrogen deficiency after menopause. 7) Prevention of osteoporosis should be targeted not only at maximizing bone mass but also restoring normal bone turnover (bone remodeling). 8) If our recommendation of the regimen consisting of adequate Ca and vit-D nutrition, exposure to sunlight, regular weight bearing exercise, vegetarian diets, avoidance of detrimental lifestyle habits and prevention from fall is recognized and appreciated, more than 90% of the burden of osteoporosis shall be eliminated from India. This regime is community acceptable and assures continuing life-term accretion of bone mass. 9) Osteoporosis is emerging an important public health problem in India with trends of rapid urbanization, and new occupational structures (factories and not farms) and increasing exposure to injurious lifestyle factors, imposing threat to National Bone Health within steadily increasing aging population. 10) Prevention of osteoporosis are our priorities in national context.

Osteoporosis may result from a reduced accumulation of bone mass during skeletal growth and consolidation or from an accelerated rate of bone loss later in life. The low peak bone mass (PBM) is a major determinant of the subsequent risk of osteoporotic fracture. More than 50% of the variability in the PBM may be explained by genetic factors, it still leaves a significant proportion determined by environmental factors and thus potentially open to manipulation. About 75% of the skeletal mass is already accumulated by late adolescence. Thus in order to prevent the development of osteoporosis, it is important to pay attention to environmental factors that contribute to bone mass gain during infancy, adolescence and young adulthood. Time has changed and osteoporosis has come to India and is set to emerge as a major public health issue. Prevention, therefore, are our priorities.
In this communication, therefore, we shall focus on the impact of environmental factors. Calcium, Vit-D (exposure to sunlight (UVR-B 290-315 nm)) and exercise in the acquisition of peak bone mass and the prevention of bone loss subsequently in the menopause.

Our Experience
Osteoporosis, the most common bone disease in postmenopausal women, is characterized by an absolute decrease in the bone mass per unit volume of bone, with a normal ratio of mineral to matrix and the mechanical stability of the skeleton is structurally compromised and weakened to the point where fractures (low energy fragility fractures) occur spontaneously or after trivial trauma. Although bone mass determines about 70% of bone strength, bone quality which can be defined as the ability of the skeleton to withstand force and not fracture is also important. Thus osteoporosis is a condition of reduced bone quantity and quality with high bone turnover (increased remodeling) that predisposes to fractures. WHO criteria for the diagnosis of osteoporosis based on the measurements of bone mineral density (BMD) and authors’ comparative cutoff diagnostic BMD values in each category of the evolution of osteoporosis are summarized (Table 1). Reports on osteoporosis in Indian literature are sparse1-12.

It is the PBM attained during skeletal growth, maturity and the young adulthood which is the major determinant of the rate of bone loss and fracture risk subsequently in the postmenopausal state (Fig 1). Bone mass is near to its maximum by 20 years of age, with a slow site-specific increase until 30 years of age, and subsequently declines in both sexes, but more rapidly in the first decade after menopause. Based on the state of bone turnover two distinct syndromes of osteoporosis type-1 and type-2 have been identified13 (Fig 2). Identifying women at greatest risk of developing osteoporotic fractures is best achieved by periodic measurement of bone mineral density and biochemical markers of bone turnover. We had previously reported that postmenopausal women with sedentary habits had a higher incidence of femoral fractures as compared to women undertaking hard physical activity2,5,6,11. The present study, therefore, was designed to further assess the independent and combined effects of calcium (Ca), vit-D and physical activity (PA) on the bone mineral content (BMC g/cm), BMD g/cm² and the rate of bone loss subsequently in the menopause.

Subjects and Methods
The authors had surveyed 337.69 million populations in 22 states of India during the period 1963-2003

<table>
<thead>
<tr>
<th>Category</th>
<th>WHO Criteria</th>
<th>*Comparative Cut Off Diagnostic BMD Values g/CM²</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td>BMD within 1 SD of Young Adult Mean (YAM)</td>
<td>Hard Work 0.982 ± 0.118</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sedentary 0.771 ± 0.112</td>
</tr>
<tr>
<td>OSTEOPENIA</td>
<td>BMD &gt; 1 SD BUT &lt; 2.5 SD Below YAM</td>
<td>0.610 ± 0.047</td>
</tr>
<tr>
<td>OSTEOPOROSIS</td>
<td>BMD 2.5 SD or more Below YAM</td>
<td>0.439 ± 0.033</td>
</tr>
<tr>
<td>SEVERE OSTEOPOROSIS</td>
<td>BMD 2.5 SD or more Below YAM and Frailty Fractures</td>
<td>0.315 ± 0.054</td>
</tr>
</tbody>
</table>

* Based on author’s personal research and extensive experience.
Fig. 1. Peak bone mass in adolescent and young adults and coupling defects in bone remodeling in postmenopausal osteoporosis, Type-1 (high bone turnover) and Type-2 (low bone turnover).

Fig. 2. Histomorphometric pictures of undeclacified double tetracycline labelled iliac crest biopsies from women with osteoporosis. Type 1 - High bone turnover, normal osteoid and clear double tetracycline labels. Type 2 - Low bone turnover, thin osteoid seam and thin tetracycline labels. 80x

for the epidemiology of the disorders of calcium and bone metabolism. From the epidemiological survey data, as a result of volunteering and exclusion criteria, only 26,600 (rural domestic), 24,500 (urban citypools), 4280 (urban westernized) and 17,100 (rural hard work) all in the age range of 20-90 yrs were recruited for the present study. These subjects were included in the study designed to investigate the role of calcium, Vit-D, and physical activity on the bone mass in specific age groups from 20-90 yrs of age. Also the validation epidemiological study on the clinical and radiological prevalence
of osteoporosis was carried out to further verify the practical information emerged on the role of environmental factors in the prevention of osteoporosis. Excluded were the females with established endocrine disorders and secondary causes of osteoporosis and those taking drugs that could affect the bone and bone mineral metabolism. BMD measurements were made at the site ultra distal radius (75% trabecular bone) of the non-dominant arm with single energy x-ray absorptiometry (SXA) and of lumbar spine L₁ – L₄ using dual energy X-ray absorptiometry (DXA).

Current, Past and Life-time Calcium Intake Assessment
Each participant was interviewed by the trained dietician and was asked to keep a-3-day dietary intake record that included the most commonly consumed dairy products as well as a non-dairy source of calcium. Dietary evaluation, in particular for Ca, vit-D and protein intakes was performed as per Indian Council of Medical Research standards. For the assessment of past Ca intakes, further questions were directed at the typical Ca intakes covering the same dairy rich foods in the past years. All subjects were enquired into whether they consumed more, the same or less of these foods and beverage item. If consumption during the past years amounted to 4 glasses of milk per day (4 x 250ml), the subjects were considered to be of normal Ca intake, if 3 glasses of milk, of low normal and if less than 2 glasses per day, of low Ca intake. Current Ca intake was combined with past Ca intake to yield a lifetime Ca intake and classified as normal, low normal and low. Vit-D nutrition was assessed on the basis of exposure to direct sunlight in the morning hours. Minimum 60 minutes of exposure per day was considered sufficient to synthesize the daily requirement (400-800 iu) of vit-D₃.

Physical Activity (PA)
Was classified as 1) Sedentary (low PA) if a subject engaged in < 2 hour/ week in a moderate intensity activity i.e. one that could bring about an elevation of the heart rate such as walking. 2) Active (high PA) if a subject performed > 60 minutes a moderate to strenuous activity minimum 4 times a week such as jogging or running, biking, weight lifting, tennis etc., 3) Hard working – spending minimum 4 hrs per day in performing very hard and strenuous work and included the females engaged in mechanical, head loading, gravity resistant and weight bearing activity such as agricultural labour, wandering tribal blacksmiths, kiln (bricks manufacturing labour), building construction labour, mountainous women (climbing minimum 5-10 km per day). The life-time PA was created from the combination of the past and current PA.

Results:
In Study 1 (Fig. 3) : Lumbar (L1-L4) BMD g/cm², in women with hard work (N=609) was compared to those with sedentary life style (N=637). The peak BMD at the age 20, and its subsequent preservation until the age of 90 years was significantly greater (P<0.001), in women with hard physical work (BMD 0.982 SD ± 0.118 g/cm²) as compared to those with sedentary habits (BMD 0.774 SD ± 0.172 g/cm²). This occurred despite the low calcium intakes (median 400 mg / day) by hard working women as compared to those with sedentary habits (median 700 mg / day). The subsequent loss of bone in hard working women was slowed and did not enter the fracture zone until 90 years of their age as compared to sedentary women who revealed accelerated immediately postmenopausal bone loss and entered the fracture zone at the age of 65 years. These observations suggested, physical activity as the most important factor in the acquisition of peak bone mass, that can offset the metabolic consequences, both, of calcium and estrogen deficiency. The hard working and sedentary women had comparable exposures to sunlight (endogenous skin synthesized D3). It is the attainment of high PBM in women with hard work that stabilized their bone mass in adulthood and slowing of bone loss subsequently in menopause.

In Study 2 (Fig 4) : CA balance studies were performed in a postmenopausal women aged 65
Fig. 3: Lumber BMD measurements in women with hard work as compared to those with sedentary habits. Women with hard work had significantly higher BMD values ($0.982 \text{ SD} + 0.118 \text{ g/cm}^2$) as compared to those with sedentary habits ($0.771 \text{ SD} + 0.112 \text{ g/cm}^2$), $P<0.001$. Women with hard work did not enter the fracture zone until 90 yrs of their age as compared to sedentary women who entered fracture zone at the age 60 yrs.

Fig. 4: Calcium balance studies in a patient with postmenopausal osteoporosis aged 65 yrs. Supplementation of calcium improved the calcium balance by decreasing urinary calcium excretion, calcium balance further improved on the addition of calcitriol with a decrease in the fecal excretion of CA.
years. Ca balances were performed on the fixed diet over three metabolic periods of six days each. Period 1 diet alone, served as a control, Period 2, calcium supplementation 1000 mg/day and Period 3 Ca 1000 mg/day plus calcitriol 0.25 µg/day. The markedly negative Ca balance, with high urinary and fecal calcium excretion in the control period improved on the addition of calcium, with reduction in the 24-hour urinary excretion of calcium. The Ca balance further improved on the addition of calcitriol in period 3. This study provided reasonable proof that the both calcium and calcitriol separately and combined markedly increase the retention of Ca and so the bone mass.

In Study 3 (Fig 5) : In this study we had measured the BMD g/cm² at the site ultra distal radius in two groups of women (age 20-90 yrs), Group-A who consumed the milk life-time and Group-B who consumed less or no milk, both groups had similar physical activity. In Group-A median Ca intake was 800 mg per/day (520 – 980 mg) and in Group-B median Ca intake was 480 mg/day (380 – 675 mg). In each age group BMD was measured in 78-92 females. The PBM and its subsequent maintenance in the later life was significantly greater in females of group-A (P<0.05). The beneficial effects of Ca intake were evident, as the females with adequate intakes entered the osteoporosis and the fracture zones at about 10 years later than those with inadequate intakes.

In Study 4 (Fig 6) : This was not the component of the study originally designed but we availed the opportunity to measure the bone mineral content (BMC) g/cm in two groups (65 women in each) of women (at age 60), life-term vegetarians and life-term non-vegetarians in order to assess the impact of the consumption of animal protein on BMC. The BMC was significantly greater (P<0.001) in vegetarians (BMC 1.095 SD ± 0.255 g/cm) than age matched non-vegetarians (BMC 0.734 SD ± 0.203 g/cm). Downward displacement of values is seen in non-vegetarians in (Fig 6). Radiographs of
the iliac crest biopsies (25 from each group) showed markedly decreased density and loss of cancellous bone with trabecular resorptions in the non-vegetarians.

In Study 5 (Table 4) : The validation epidemiological study was undertaken for the clinical and radiological prevalence of osteoporosis in the population recruited for study. The urbanized westernized women showed the highest incidence of thoracic kyphosis (clinical variable) and of femoral fractures (radiological variable), whereas the least incidence of osteoporosis was discovered in women with hard physical activity.

Fig. 6 : Radial BMC values (g/cm) is compared in the life-time vegetarian and non-vegetarian females at age 60 yrs. Note the down-word displacement of the data in non-vegetarian females indicating low BMC values. The mean BMC g/cm in the non-vegetarian females was 40% less than the age matched vegetarians. P<0.001 the BMC significantly greater in vegetarians than in non-vegetarians.
Table 2: The Possible Mechanisms that May Relate Physical Activity (Bone Load) to Bone Mass

<table>
<thead>
<tr>
<th>Head loading and gravity resistant exercises</th>
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<tbody>
<tr>
<td>Compression of bone surfaces,</td>
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<tr>
<td>Strain on organic matrix of bone</td>
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<tr>
<td>Electronegative potential with respect to the remaining bone</td>
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<tr>
<td>Stimulation of osteogenesis (Osteoinductive forces)</td>
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<tr>
<td>Increased synthesis of proteoglycan</td>
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<tr>
<td>Increased collagen bio-synthesis</td>
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<tr>
<td>Increased alkaline phosphatase</td>
<td>↓</td>
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<tr>
<td>Decreased bone loss, Increased formation of new bone</td>
<td>↓</td>
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<tr>
<td>Remodeling Balance</td>
<td>↓</td>
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<tr>
<td>Increased neuromuscular co-ordination,</td>
<td>↓</td>
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<tr>
<td>strength, stability, balance, protection against falls</td>
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<tr>
<td>Positive gain in bone mineral density</td>
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</table>

Discussion

This clinical study was designed to demonstrate the efficacy of Ca, vit-D, and PA in the prevention of osteoporosis and is the first of its kind on the indigenous population. Our results (Figs. 3, 4, 5) had shown that life-time, PA (weight bearing, gravity resistant, head and mechanical loading) is the first and the most effective strategy in the prevention of osteoporosis. Women in hard working group revealed significantly greater acquisition of PBM at adolescence and its subsequent stabilization and preservation during adulthood and perimenopause and also had slow decline in the immediately postmenopausal bone loss (Fig. 3). The possible mechanisms that may relate bone load to bone mass have recently been reviewed. When bone is compressed or strained, the surfaces directly receiving the forces develop an electronegative potential with respect to the remaining bone. This voltage arises from a strain on the organic matrix (most likely the collagen fibrils). This electronegativity, in turn, stimulates osteogenesis (Table 2).

The adequate life-time Ca nutrition is the second effective strategy with its beneficial influence on the achievement of PBM, its maintenance in adult females and its optimization and slow decline subsequently in later life. Calcium supplementation’s did not completely arrest post-menopausal bone loss but slowed the rate of decline by 30-50%. The recommended optimal intakes include an intake of Ca of 500 mg/day for children aged 1-3 years; 800 mg/day for those 4-8 years; 1300 mg/day for those 9-18 years; 1000 mg/day from 19-50 years; and for those older than 50 years 1500 mg/day. Calcium carbonate offers the highest calcium content per unit tablet weight (40%), with calcium citrate being second at (30%). Absorption of calcium as a citrate is slightly more efficient and not dependent on gastric acidity.

All the subjects had adequate vitamin-D nutrition through daily exposure (1-4 hours) to sunlight and endogenous skin synthesis of vit-D3. In the separate study we had shown that more than 90% of the circulating serum 25-OHD is derived from skin synthesized vit-D3 and the dietary vit-D only has a
marginal or negligible role. An insufficient availability of vit-D impairs intestinal Ca absorption and bone mineralisation, increases bone resorption and turnover. Thus the low serum vit-D levels are associated with a low bone mass. Vit-D deficiency rickets and osteomalacia with associated secondary hyperparathyroidism are the commonest nutritional bone disorders in “the growing children and the mothers” of child bearing age in India. These disorders are associated with low BMD. Our observations of low bone mass (also fetal rickets) in newborns to osteomalacia mothers is the strong evidence that the seeds of osteoporosis may infact be sown in fetal life and early infancy.

Other nutritional factors important in the prevention of osteoporosis include adequacy of calorie, protein and vitamins such as vitamin-C and K and the minerals manganese, copper and zinc which are necessary cofactors for enzymes involved in the synthesis or post-translational modification of various constituents of bone matrix. Low protein intake impairs both the production and action of IGF-1, an essential factor for bone growth, stimulates osteoblastic bone formation and also stimulates production of 1,25(OH2D3). High animal protein exhausts the bone mineral stores and suppresses the production of 1,25(OH2D3) and causes the acidic metabolic stress on the body.

Table 3: Practical Risk Factors for Osteoporosis in Indian Females

<table>
<thead>
<tr>
<th>Risk Factor</th>
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<tbody>
<tr>
<td>1. Infant’s born with low bone mass, from calcium and vit-D deficient or osteomalacia mothers.</td>
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<tr>
<td>2. Lack of acquisition of peak bone mass during adolescence and at skeletal maturity (12-30 yrs. of age).</td>
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<tr>
<td>3. Premature menopause (spontaneous or surgical).</td>
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<tr>
<td>4. Early marriage and children - mothers deprived even of genetic and environmental potentials to accumulate maximal peak bone mass.</td>
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<tr>
<td>5. Life style.</td>
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<tr>
<td>Sedentary habits</td>
<td></td>
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<tr>
<td>Lack of weight bearing and antigravity exercises</td>
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<tr>
<td>Lack of exposure to sun light (UV-R-B 290-315 nm)</td>
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<tr>
<td>Emerging cigarette smoking and alcohol abuse</td>
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<tr>
<td>6. Nutrition</td>
<td></td>
<td></td>
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<tr>
<td>Dietary calcium deficiency</td>
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<td></td>
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<tr>
<td>Vit-D deficiency</td>
<td></td>
<td></td>
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<tr>
<td>Protein deficiency</td>
<td></td>
<td></td>
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<tr>
<td>Consumption of animal protein (non-veg foods)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumption of caffeine</td>
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<td></td>
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<tr>
<td>7. Bone diseases during critical years of skeletal growth</td>
<td></td>
<td></td>
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<tr>
<td>(rickets, nutritional hyperparathyroidism, osteoporosis, endemic uroasis,)</td>
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<tr>
<td>8. Clinical or Sub-clinical depletion of calcium and Vit-D stores in mothers due to repeated pregnancies and lactations.</td>
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<tr>
<td>9. Vit-D deficiency osteomalacia with secondary hyperparathyroidism in women of child bearing age (uncommon in postmenopausal women)</td>
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<tr>
<td>10. Multiparity</td>
<td></td>
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<tr>
<td>11. Associated secondary causes of osteoporosis</td>
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</tbody>
</table>

The validation epidemiological study performed revealed the highest incidence of clinical and radiological osteoporosis in the urban westernized women and osteoporosis was practically non-existent in women engaged in hard PA.
Table 4: Impact of Calcium, Vit-D and Exercise - Validation Study Epidemiology of Osteoporosis

FEMALES 50 – 90 YEARS

<table>
<thead>
<tr>
<th>Number of Subjects</th>
<th>Rural Domestic</th>
<th>Urban City pools</th>
<th>Urban • Westernized</th>
<th>Hard Working</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>26,600</td>
<td>24,500</td>
<td>4,280</td>
<td>17,100</td>
</tr>
</tbody>
</table>

Clinical (%)

- Symptomless loss of height
  - Females 50 – 90 years
    - Rural Domestic: 6.5%
    - Urban City pools: 13.8%
    - Urban • Westernized: 17.2%
    - Hard Working: 0%

- Low back pain
  - Females 50 – 90 years
    - Rural Domestic: 19.0%
    - Urban City pools: 45%
    - Urban • Westernized: 51.0%
    - Hard Working: 2.2%

- Thoracic kyphosis
  - Females 50 – 90 years
    - Rural Domestic: 1.6%
    - Urban City pools: 6.5%
    - Urban • Westernized: 9.7%
    - Hard Working: 0%

Radiological (%)

- Anterior wedging
  - Females 50 – 90 years
    - Rural Domestic: 5.5%
    - Urban City pools: 11.5%
    - Urban • Westernized: 13.9%
    - Hard Working: 0%

- Biconcavity and ballooning
  - Females 50 – 90 years
    - Rural Domestic: 12.0%
    - Urban City pools: 29%
    - Urban • Westernized: 32.2%
    - Hard Working: 1.5%

- Compression Fractures (Crush)
  - Females 50 – 90 years
    - Rural Domestic: 3.8%
    - Urban City pools: 8.8%
    - Urban • Westernized: 9.0%
    - Hard Working: 0%

- Ribs, colles, fractures
  - Females 50 – 90 years
    - Rural Domestic: 1.5%
    - Urban City pools: 5.2%
    - Urban • Westernized: 5.8%
    - Hard Working: 0%

- Femoral fractures
  - Females 50 – 90 years
    - Rural Domestic: 1.0%
    - Urban City pools: 4.8%
    - Urban • Westernized: 6.7%
    - Hard Working: 0%

- BMD g/cm² (ultra distal radius)
  - Females 50 – 90 years
    - Rural Domestic: 0.771 ± 0.112 SD, N=125
    - Urban City pools: 0.680 ± 0.047 SD, N=132
    - Urban • Westernized: 0.610 ± 0.042 SD, N=126
    - Hard Working: 0.982 ± 0.118 SD, N=158

• Consumed animal protein, smoking and alcohol

We recommend that the practical targets for prevention of osteoporosis should be directed at:

1) The pregnant and lactating mothers to give birth to babies with normal bone mass.
2) Developing strong bones in teenage.
3) Achieving PBM during adolescence.
4) Preserving bone mass in young adult females of child bearing age.
5) Optimizing bone mass in perimenopause.
6) Prevention of bone loss after menopause.

All these states are positively related to adequate intakes of Ca, vit-D and exercise. Elemental Ca 1000-1500 mg, vit-D 400-800 iu/day is the most effective regime recommended. Vit-D metabolites and pharmacologic intervention for preventing bone loss are recommended only with specific reasons.

A) Bones “Breathe” in sun, “Grow” on calcium, gain “Strength” in action.
B) Pregnancy “Licks” the bones, lactation “Kicks” the bones, and animal protein “Robs” the bones.

Authors’ slogans look appropriate to create awareness of osteoporosis in the community and to emphasize the role of Ca, vit-D and exercise in its prevention.

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Acknowledgement

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