Osteoporosis in India

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Member, CSA, International Osteoporosis Foundation
Member Executive, Bone and Joint Decade
President, Indian Society for Bone and Mineral Research
Osteoporosis is a systemic skeletal disease characterized by *low bone mass* and *microarchitectural deterioration* of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.


Image: Courtesy Dr. A. Boyde
Hip Fractures

*Hip fracture is associated with increased risk of:*

- Disability: 50% never fully recover
- Long-term nursing home care required: 25%
- Increased mortality within 1 year: up to 24%
- Lifetime risk of death: comparable to that of breast cancer
Osteoporotic Fractures in Women, Compared With Other Diseases

1,200,000
513,000
228,000
184,300

Osteoporotic Fractures
Heart Attack
Stroke
Breast Cancer

Risk of Another Vertebral Fracture Is Higher in the Year Following a New Fracture

- Overall, ~20% fractured again within the year following a new fracture
- Risk of fracture increased with the number of baseline fractures

*p<0.05, vs patients with no prevalent vertebral fractures (12-fold increased risk).
Pilot Case-Control Investigation of Risk Factors for Hip Fractures in the Urban Indian Population

Ruchira M. Jha, B.A #.*, Ambrish Mithal, M.D,D.M.#, Edward Brown, M.D.*

#Indraprastha Apollo Hospital, New Delhi, and
*Brigham and Women’s Hospital, Boston
Methods

- 100 case subjects were those admitted with a first hip fracture into one of three hospitals across Delhi.
- The 100 controls were age and sex matched subjects who were either hospital staff, or healthy visitors not related to the case patients.
- Information from all subjects was obtained through a questionnaire based interview.
- The importance of risk factors for hip fractures was assessed with univariate and multivariate logistic regression.
Lifestyle factors

- Active persons (defined as those with activity level >2) have a 97.6% lower risk of hip fracture.
- An increase of 1 in BMI resulted in an 18.6% reduced risk of hip fracture.
- Decreased agility (difficulty in getting up from a chair) raised the chance of hip fracture.
Dietary factors

- All calcium containing food items (paneer, milk, curd) and calcium supplements had protective effect on hip fracture.
- Dietary vitamin D (almonds, fish) also reduced the risk of hip fracture.
- Regular tea drinkers and persons who drank other caffeinated beverages were at a higher risk of hip fracture.
Number of cases presenting with a light fall, pain, or a car accident.

**DISTRIBUTION OF FRACTURE PRESENTATION MODES**

- **Total**: 85
- **Male**: 35 (Pain: 5, Car Accident: 3)
- **Female**: 51 (Pain: 6, Car Accident: 1)

August 1, 2007

NFI
BODY MASS INDEX OF 100 CASES AND 100 CONTROLS

Number of cases/control

BMI Status

- BMI < 22.7
- BMI 22.71-24.4
- BMI > 24.41

Case
Control

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MEDICATIONS OF 100 CASES AND 100 CONTROLS

Number of subject (equivalent to %)

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>27</td>
<td>15</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Ashtma</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Heart Problem</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aurvedic / Homeopathic</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cardiac and Hypertension</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>AMI Diabetes</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hormons</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

August 1, 2007

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AGE DISTRIBUTION OF HIP FRACTURES

- 0-29: 5%
- 30-39: 3%
- 40-49: 9%
- 50-59: 9%
- 60-69: 30%
- 70-79: 31%
- 80-89: 4%
- 90-99: 9%
- NFI: 5%
## MULTIVARIATE ANALYSIS OF RISK FRACTURES FOR HIP FRACTURE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Persons</td>
<td>0.024 (0.006-0.10)</td>
<td>0.000</td>
</tr>
<tr>
<td>Take Calcium Supplements</td>
<td>0.076 (0.017-0.340)</td>
<td>0.001</td>
</tr>
<tr>
<td>Eat Paneer</td>
<td>0.152 (0.031-0.741)</td>
<td>0.020</td>
</tr>
<tr>
<td>Eat Fish</td>
<td>0.094 (0.020-0.431)</td>
<td>0.002</td>
</tr>
<tr>
<td>Regular Tea Drinkers</td>
<td>22.81 (3.73-139.43)</td>
<td>0.001</td>
</tr>
<tr>
<td>Difficulty Getting up from Chair</td>
<td>14.53 (3.86-54.23)</td>
<td>0.000</td>
</tr>
<tr>
<td>Age</td>
<td>0.92 (0.88-0.97)</td>
<td>0.000</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>0.81 (0.68-0.97)</td>
<td>0.021</td>
</tr>
</tbody>
</table>
Conclusions

- Calcium, vitamin D, increased body mass index, and higher activity levels have a significant protective effect on hip fracture in the urban north Indian population.

- Caffeine intake and decreased agility increases the risk of hip fracture.
BMD in Indians

- Total studies – 15
- Total no. of subjects/Pts studied – 1332
  *for population of >1 billion!*

- Total studies for migrant Indians – 39
- Total no. of subjects/Pts studied - 855
Sites of studies of BMD in India
Study from Apollo Hospital, ND

- 289 women in the age group of 20-84 yrs
- Each decade – 35-40 healthy females
- Secondary diseases excluded
- Peak BMD – 3rd decade – 1.05gm/cm² spine
- 24% decline in BMD up to 7th decade
- Mean spine & hip BMD – significantly lower than Caucasian

Uma R, in Osteoporosis by Balu Shankaran 2002
AIIMS- INMAS Delhi study

- 40 young healthy male & 50 young healthy female
- Secondary diseases excluded
- Daily calcium intake - >700 mg
- Adequate sun exposure
- All were vitamin D sufficient with normal PTH
- BMD – DXA at spine and hip

Marwaha RK et al NMJI 2002
Delhi study

- No significant difference in BMD between Indian female & Caucasian female
- Significantly lower spine BMD in Indian male than Caucasians data
- Other places, no significant difference
- Weight – positive correlate in female
- Daily calcium intake – positive correlate in male
Vitamin D status and its relationship with bone mineral density in healthy Asian Indians

Vivek Arya · Rajiv Bhandari · Madan M. Godbole
Ambrish Mithal
Serum vitamin D status
Healthy Hospital Staff – SGPGI

Serum 25(OH) D level (ng/ml)

Arya V, Mithal A et. al. Osteoporosis International:15:56-61, 2004
Spinal BMD in normal Indian females

Mean BMD g/sq. cm

Age group

20-29  30-39  40-49  50-59

NORTH AMERICAN  JAPANESE  INDIAN

Peak BMD of Indians: Data from India vs US Caucasians

(Studies performed on Hologic QDR machines.)

BMD (g/cm²)

- Delhi
- Chennai
- Lucknow
- U.S. Whites

- AP Spine
- LFN

ASBMR, 2004
Peak BMD of Indians – across the world

ASBMR, 2004
Effect of database on diagnosis of osteoporosis in expatriate (US) Indians.

Effect of Database on diagnosis of osteoporosis (WHO criteria).
Taken from Honasoge et al. OPO = osteoporosis; OPE = osteopenia.

ASBMR, 2004
Why is calcium nutrition important?

In our studies on hospital staff, 74% of subjects had calcium intake below 500mg/day!
Correlation between 25(OH)D & BMD of femoral neck

Arya, Mithal.. Osteoporosis Intl, Jan 2004

R = 0.47
p = 0.04
Possible that this data reflects poor bone health of Indians.

Till more definitive data becomes available, is it prudent to use this data to diagnose osteoporosis in Asian Indians across the globe ????
Spine BMD in 974 healthy Indian women using Lunar DXA: Comparison with Caucasian database

Endocrine Society, 2004
Femoral neck BMD in 911 healthy Indian women using Lunar DXA: Comparison with Caucasian database

Endocrine Society, 2004
Bone status of Indian women – low income group - NIN study

- 289 women in the 30-60 years age gp.
- Non-pregnant, non-lactating ladies from large urban slum in Hyderabad

- BMD – hip, spine, forearm & whole body
- Vitamin D – not estimated

Veena Shatrugna et al Osteoporosis Int. 2005
## NIN study

<table>
<thead>
<tr>
<th>Area</th>
<th>BMC</th>
<th>BMD</th>
<th>T score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur Neck</td>
<td>2.84</td>
<td>0.712</td>
<td>-1.81</td>
</tr>
<tr>
<td>Hip</td>
<td>21.3</td>
<td>0.769</td>
<td>-1.71</td>
</tr>
<tr>
<td>Spine</td>
<td>37.8</td>
<td>0.797</td>
<td>-2.27</td>
</tr>
<tr>
<td>Arm</td>
<td>9.29</td>
<td>0.486</td>
<td>-1.53</td>
</tr>
<tr>
<td>Whole body</td>
<td>1,561</td>
<td>0.999</td>
<td>-</td>
</tr>
</tbody>
</table>

- All - significantly lower than Caucasians
**NIN study**

- Prevalence of osteoporosis & osteopenia – WHO criteria

<table>
<thead>
<tr>
<th>Area</th>
<th>Porosis</th>
<th>Penia</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>F Neck</td>
<td>29%</td>
<td>52%</td>
<td>19%</td>
</tr>
<tr>
<td>Spine</td>
<td>43%</td>
<td>43%</td>
<td>14%</td>
</tr>
</tbody>
</table>
Studies in 2006

- Bone health & VDR gene polymorphism
  
  *Vupputuri, Goswami et al, Am J Clin nutr 2006*

- VDR gene polymorphism in PM women

  *Mitra et al, Maturitas 2006*

- ER gene polymorphism in PM women

  *Mitra et al, Mol Genet Metab 2006*

- Effect of micronutrient supplement on bone health of school children

  *Shatrugan et al, Nutrition 2006*
DXA facility in India

- First DXA machine in India 1997 – SGPGI, Lucknow
- Total 125 -130 DXA all over India
- Majority – private sector
- Costly equipment and investigation
- ? Portable central DXA
ICMR study: four centers

- ALIMS
- SGPGI
- NIRRH
- NIN
Effect of vitamin D supplementation on bone mineral health of young healthy females.

Indraprastha Apollo Delhi,
SGPGIMS, Lucknow
Objectives

• To confirm the efficacy of once monthly dose of oral vitamin D in healthy young females.

• Effect of supplementation on biochemical parameters and BMD.
Study design

- Prospective, randomised, controlled study
- 100 healthy young adult females (hospital staff) were recruited.
- Study subjects were randomised into two equal groups by simple randomisation.
- Group A was the control group and group B received monthly doses of vitamin D (Calcirol 60,000 IU).
- Baseline samples were drawn for serum calcium, phosphorus, alkaline phosphatase, creatinine, PTH, vitamin D levels, urine calcium, phosphorus, and creatinine.
- Blood and urine samples to be repeated after 3mo, 6mo and 12mo.
- Baseline BMD was measured by DXA, to be repeated after 1yr.
# Baseline values

<table>
<thead>
<tr>
<th></th>
<th>25 (OH) D (ng/ml)</th>
<th>Intact PTH (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td><strong>Minimum</strong></td>
<td>0.23</td>
<td>17.23</td>
</tr>
<tr>
<td><strong>Maximum</strong></td>
<td>17.13</td>
<td>146.00</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>16.90</td>
<td>128.77</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>4.5577</td>
<td>50.0334</td>
</tr>
<tr>
<td><strong>Std. Deviation</strong></td>
<td>3.15885</td>
<td>25.52077</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>4.2050</td>
<td>44.9450</td>
</tr>
<tr>
<td><strong>Std. Error of Mean</strong></td>
<td>0.31588</td>
<td>2.60470</td>
</tr>
</tbody>
</table>
SCATTER DIAGRAM BETWEEN VITAMIN D AND PTH

VITAMIN D vs. INTACT PTH

The scatter plot shows a negative correlation between vitamin D and intact PTH levels. The points are scattered across the graph, with some clustering towards the upper left, indicating higher PTH levels with lower vitamin D levels. A trend line is superimposed on the plot, which suggests a downward trend as vitamin D levels increase.
Box Plot of Intact PTH under different categories of Vitamin D

- Intact PTH (pg/ml)
- Vit D (ng/ml)

Categories:
- >15
- 9-12
- 6-9
- 3-6
- 0-3

Vitamin D levels and corresponding Intact PTH values are depicted in the box plot.
Changes in BMD during treatment of osteomalacia

Figure 3: Percent change in BMD of lumbar spine (n = 9)

Bhambhri R, Naik V, Malhotra N, Mithal A.
J Clin Densitometry, 9:120127, 2006
Figure 4: Percent change in BMD of femoral neck (n = 9)

Bhambhri R, Naik V, Malhotra N, Mithal A.
J Clin Densitometry, 9:120127, 2006
Figure 5: Percent change in BMD of forearm (n = 4)

Bhambhri R, Naik V, Malhotra N, Mithal A.
J Clin Densitometry, 9:120127, 2006
CONCLUSION

• Serial BMD measurements can assess the initial severity of bone loss, response to and compliance with therapy.

• *With treatment there are large increases in vertebral and hip BMD.*

• *Similar gains in BMD are however not seen at sites such as the forearm* as the cortical thinning due to secondary hyperparathyroidism may be irreversible.
Question 1

- What is the prevalence of osteoporotic fractures among Indians? How does this rate compare with that in the western populations?
Question 2

- What BMD cut off should be used to diagnose Osteoporosis for the Indian population?
- Should we use an Indian reference range and what fracture threshold should we use?
- What are the implications of using different BMD cut offs?
Question 3

- To what extent does calcium and vitamin D deficiency play a role in the reported low BMD and presumed higher fracture rates among Indians?
Question 4

- Is the response of Indian to various anti-osteoporotic therapies including calcium and vitamin D different than that reported for other populations?
Indian Society for Bone and Mineral Research

3rd annual conference
AIIMS, 29/30th sept
(also first South Asian Bone Mineral Meeting)

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