Multi-Pronged Strategy to combat Vitamin D deficiency in India

C Ramachandran Memorial Lecture

by

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INTERNATIONAL LIFE SCIENCES INSTITUTE (ILSI), INDIA & Advisor
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DEPT. OF ENDOCRINOLOGY AND THYROID RESEARCH CENTRE
INMAS, DRDO, DELHI
• Vitamin D is an important hormone necessary not only for maintaining calcium balance and safeguarding skeletal integrity but also essential for overall health and well being.

• Primarily acquired by exposure to sunlight.

• Food articles commonly consumed by Indians do not provide adequate vitamin D.

• No food articles are adequately fortified in India.

• The most sensitive index in assessing vitamin D status is 25(OH)D

• Nutritional rickets and vitamin D deficiency continues to exist as a major health problem in India.
Why Sound Bone Health?

- Poor bone health is responsible for causation of 8.9 million Fractures annually worldwide.

- Life time risk for hip, vertebral and wrist fracture is 30-40%.

- High morbidity and mortality associated with osteoporotic fractures.
Projected Number of Osteoporotic Hip Fractures Worldwide

Estimated number of hip fractures: (1000s)

- **1950**
  - **1950**: 378
  - **2050**: 742

- **2050**
  - **1950**: 100
  - **2050**: 668

- **2050**
  - **1950**: 600
  - **2050**: 3250

**Total number of hip fractures:**
- **1950** = 1.66 million
- **2050** = 6.26 million

Projected to reach **3.250 million** in Asia by 2050

Adapted from C. Cooper et al, Osteoporos Int. 1992; 2:285-9
All Fractures are Associated with Morbidity

One year after a hip fracture:

- Death within one year: 20%
- Permanent disability: 30%
- Unable to walk independently: 40%
- Unable to carry out at least one independent activity of daily living: 80%

Should we bother about serum vitamin D levels?
Adverse effects of Vitamin-D Deficiency

**Vitamin D deficiency/insufficiency in Pregnancy & Lactation:**

- Adverse maternal outcomes like Osteomalacia and Preeclampsia
- Lower birth weight
- Lower crown heel length, head circumference and mild arm circumference
- Low bone mass
- Poor/ delayed Growth
- Rickets in utero/ at birth
- Tetany
- Neonatal hypocalcemic seizures
- Abnormal enamel formation and dental caries
ADVERSE EFFECTS OF VITAMIN D DEFICIENCY

Children and adolescents:
- Poor growth velocity
- Rickets
- Short stature
- Low bone mass
- Genu Varum (Bow legs)
- Genu Valgum (Knock knees)
- Respiratory viral infections (including swine flu)

Adult & old age:
- Muscle pain & fatigue
- Osteomalacia
- Osteoporosis
- Hip, Spine, Forearm and other fractures.
- Increase prevalence of autoimmune disorders, cardiovascular diseases, skin disorders, cancers and infections.
Extra-skeletal Benefits

- It is a potent immune system modulator and prevents development of autoimmune disorders and respiratory infections like influenza virus.

- It inhibits uncontrolled proliferation and stimulates differentiation of cells thereby preventing common cancers and skin disorders.

- Plays a role in insulin secretion under conditions of increased insulin demand and increases insulin sensitivity.

- Decreases cardiovascular mortality.

*Whiting J S and Calvo S M* American Society of Nutritional Sciences, 2005
Vitamin D- Published Strength of Evidence
WHY DO I CALL IT A WONDER VITAMIN?
Vitamin D: A New Promising Therapy for Congenital Ichthyosis.

Sethuraman G¹, Marwaha RK², Challa A³, Yenamandra VK³, Ramakrishnan L⁴, Thulka S⁵, Sharma VK³.

Abstract

Severe vitamin D deficiency and rickets are highly prevalent among children with congenital ichthyosis. We report an incidental observation of a dramatic and excellent clinical response with regard to skin scaling and stiffness in children with congenital ichthyosis after short-term high-dose vitamin D supplementation that has not been previously described. Seven children with congenital ichthyosis (5 with autosomal recessive congenital ichthyosis; 2 with epidermolytic ichthyosis) and severe vitamin D deficiency (and/or rickets) were given 60,000 IU of oral cholecalciferol daily for 10 days under supervision. All children were subsequently put on recommended daily allowance of 400 to 600 IU of cholecalciferol. The main outcome measures observed and studied were reduction in skin scaling and stiffness of the extremities. All cases had severe vitamin D deficiency (serum 25-hydroxyvitamin D < 4 ng/mL) and secondary hyperparathyroidism. Six patients had clinical and radiologic evidence of rickets. Significant improvement in scaling was noticeable by day 5, showing further improvement by day 10, in 6 of the 7 cases. At 1 month, the skin had become near normal in all the cases of autosomal recessive congenital ichthyosis. Remarkable reduction in stiffness was also observed in all children. Supplementation with high-dose vitamin D followed by recommended daily allowance appears to be an effective form of therapy in the management of congenital ichthyosis with vitamin D deficiency.

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PMID: 26721572 DOI: 10.1542/peds.2015-1313
BACKGROUND:
Hypocalcaemia accounts for a majority of seizures in infants reporting to the emergency ward of our hospital.

OBJECTIVE:
To evaluate the role of Vitamin D deficiency in the etiology of hypocalcemic seizures in infancy.

DESIGN AND SETTING:
Cross sectional hospital based study, from April 2006-March 2007.

SUBJECTS:
60 infants with hypocalcemic seizures and their mothers (study group) and 60 healthy breastfed infants with their lactating mothers (control group).

MEASUREMENTS:
Vitamin D [25(OH) D] and intact para-thormone levels.


Conclusion

- Infants born to vitamin deficient mothers are at a significantly higher risk of developing hypocalcemic seizures.
There is scarcity of data on the effect of vitamin D deficiency (VDD) on muscle energy metabolism. The study recruited 19 healthy subjects with low serum 25(OH)D levels (<5 ng/mL). Subjects supplemented with cholecalciferol at a dose of 60,000 IU/week for 12 weeks. Prevalence of low phosphocreatine/inorganic phosphate (PCr/Pi) ratio and high phosphodiester (PDE) values in normal Indian population may be attributed to vitamin D deficiency. Serum 25(OH)D level plays an important role in improving the skeletal muscle energy metabolism.
Results & Conclusion

- Significant improvement in PCr/Pi ratio ($p=0.01$) and marked reduction of PDE/ATP ($p=0.04$) and Pi/ATP (0.04) based on $^{31}$P MRS after 12 wks of vitamin D supplementation was observed.

- These results indicate serum 25 (OH)D level plays an important role in improving the skeletal muscle energy metabolism.
BONE HEALTH IN HEALTHY INDIAN POPULATION AGED 50 YEARS AND ABOVE

Marwaha R K et al. Osteoporosis International 2011; 22, 2829-36
Establishment of Age-Specified Bone Mineral Density Reference Range for Indian Females Using Dual-Energy X-Ray Absorptiometry

Raman K. Marwaha,* 1 Nikhil Tandon, 2 Parjeet Kaur, 2 Aparna Sastry, 1 Kuntal Bhadra, 1 Archna Narang, 1 Saurav Arora, 1 and Kalaivani Mani 3

1Department of Endocrinology and Thyroid Research Centre, Institute of Nuclear Medicine and Allied Sciences, New Delhi, India; 2Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India; and 3Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India
Comparison of reference NHANES III and Hologic reference standards with Indian Standards

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex</th>
<th>Total Hip</th>
<th>Forearm</th>
<th>Lumbar Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES III</td>
<td>Male</td>
<td>1.041±0.144</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>0.942±0.122</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>HOLOGIC</td>
<td>Male</td>
<td>----</td>
<td>0.679±0.054</td>
<td>1.121±0.110</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>----</td>
<td>0.564±0.051</td>
<td>1.084±0.111</td>
</tr>
<tr>
<td>INDIANS</td>
<td>Male (404)</td>
<td>0.988±0.131</td>
<td>0.611±0.052</td>
<td>0.976±0.105</td>
</tr>
<tr>
<td></td>
<td>Female (404)</td>
<td>0.901±0.111</td>
<td>0.538±0.044</td>
<td>0.954±0.095</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt; 0.01</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>
## Comparison of mean BMD values in Healthy & apparently healthy Indian Males

(20-30 yrs)

<table>
<thead>
<tr>
<th></th>
<th>Jawans study (Lunar)</th>
<th>Lucknow study (Lunar)</th>
<th>ICMR Study (Hologic)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong></td>
<td>173 cm</td>
<td>172.5 cms</td>
<td>172 cms</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>68.8 kgs</td>
<td>65.1 kgs</td>
<td>67 kgs</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>22.8</td>
<td>21.3</td>
<td>22.6</td>
</tr>
<tr>
<td><strong>Total Hip BMD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 – 30 years</td>
<td>1.142 (0.128)</td>
<td>1.018 (0.133)</td>
<td>0.988 (0.131)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>p&lt;0.001</strong></td>
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<tr>
<td><strong>Femur Neck BMD</strong></td>
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</tr>
<tr>
<td>20-30 years</td>
<td>1.130 (0.127)</td>
<td>1.019 (0.131)</td>
<td>0.894 (0.131)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>p&lt;0.001</strong></td>
</tr>
<tr>
<td><strong>Femur Trochanter BMD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-30 years</td>
<td>0.936 (0.132)</td>
<td>0.859 (0.114)</td>
<td>0.723 (0.113)</td>
</tr>
<tr>
<td><strong>Radius 33% BMD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-30 years</td>
<td>0.748 (0.72)</td>
<td>0.891 (0.085)</td>
<td>0.725 (0.062)</td>
</tr>
<tr>
<td><strong>Radius UD BMD</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>20-30 years</td>
<td>0.451 (0.080)</td>
<td>0.525 (0.064)</td>
<td>0.465 (0.054)</td>
</tr>
<tr>
<td><strong>L1-L4 BMD</strong></td>
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<tr>
<td>20-30 years</td>
<td>1.175 (0.134)</td>
<td>0.531 (0.065)</td>
<td>0.976 (0.105)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>p&lt;0.001</strong></td>
</tr>
</tbody>
</table>
RESULTS

- **Prevalence of Osteoporosis:**
  562 subjects (35.1%) [M-24.8%; F-42.5%]

- **Prevalence of Osteopenia:**
  792 subjects (49.5%) [M-54.3%; F-44.9%]

Prevalence of osteoporosis increased significantly with age.
ASSESSMENT OF LEAN MUSCLE MASS AND IT’S DISTRIBUTION BY DXA IN HEALTHY INDIAN FEMALES

Maj Gen (Dr)) RK Marwaha
Former Additional Director and head, Dept of Endocrinology and Thyroid Research Centre, INMAS, DRDO, MOD
Presently Scientific Advisor and Senior consultant Endocrinology International Life Sciences Institute, ILSI (India)
## Comparison of lean mass in the present study with data from NHANES (1999-2004)

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>NHANES (1999-2004)</th>
<th>Present Study</th>
<th>Difference</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Mean</td>
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<tr>
<td>Total Lean Mass (Kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-19</td>
<td>39.6</td>
<td>32.6*</td>
<td>-21.5</td>
<td></td>
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<tr>
<td>20-39</td>
<td>42.3</td>
<td>34.8</td>
<td>-21.6</td>
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<tr>
<td>40-59</td>
<td>43.0</td>
<td>34.6</td>
<td>-24.3</td>
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<tr>
<td>60-79</td>
<td>40.3</td>
<td>32.8</td>
<td>-22.9</td>
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</tr>
<tr>
<td>Leg Lean Mass (Kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-19</td>
<td>13.1</td>
<td>11.0*</td>
<td>-19.1</td>
<td></td>
</tr>
<tr>
<td>20-39</td>
<td>13.8</td>
<td>11.6</td>
<td>-19.0</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>13.7</td>
<td>10.7</td>
<td>-28.0</td>
<td></td>
</tr>
<tr>
<td>60-79</td>
<td>12.5</td>
<td>9.8</td>
<td>-27.6</td>
<td></td>
</tr>
<tr>
<td>Arm Lean Mass (Kg)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>16-19</td>
<td>3.9</td>
<td>3.3*</td>
<td>-18.2</td>
<td></td>
</tr>
<tr>
<td>20-39</td>
<td>4.3</td>
<td>3.7</td>
<td>-16.2</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>4.4</td>
<td>3.5</td>
<td>-25.7</td>
<td></td>
</tr>
<tr>
<td>60-79</td>
<td>3.9</td>
<td>3.3</td>
<td>-18.2</td>
<td></td>
</tr>
<tr>
<td>Trunk Lean Mass (Kg)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>16-19</td>
<td>19.5</td>
<td>15.4*</td>
<td>-26.6</td>
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</tr>
<tr>
<td>20-39</td>
<td>21.1</td>
<td>16.7</td>
<td>-26.3</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>21.9</td>
<td>17.7</td>
<td>-23.7</td>
<td></td>
</tr>
<tr>
<td>60-79</td>
<td>20.8</td>
<td>17.1</td>
<td>-21.6</td>
<td></td>
</tr>
</tbody>
</table>

* In the present study this age group was from 18-20 years
Conclusion

- Indian women had lower muscle mass when compared with Caucasian by 15-28% (Borrud LG 2010) and Chinese (9%) counterparts (Cheng Q 2013).

- These differences can probably be explained by racial, anthropometric and life style factors (diet & physical activity).

- Early menopause in Indian women when compared to their Caucasian counterparts (Singh M et al 2012, Kto I et al 1998) may also contribute to lower lean mass in older women (Mithal et al 2013).
The prevalence of and risk factors for radiographic vertebral fractures in older Indian women and men: Delhi Vertebral Osteoporosis Study (DeVOS)

Raman K. Marwaha · Nikhil Tandon · Yashdeep Gupta · Kuntal Bhadra · Archana Narang · Kalaivani Mani · Ambrish Mithal · Subhash Kukreja

Received: 9 March 2012 / Accepted: 9 August 2012
© International Osteoporosis Foundation and National Osteoporosis Foundation 2012
Fig. 1  Prevalence of vertebral fractures in males and females according to age strata
Effects of sports training & nutrition on bone mineral density in young Indian healthy females


Department of Endocrinology & Thyroid Research, Institute of Nuclear Medicine & Allied Sciences, *Department of Food & Nutrition, Institute of Home Economics, University of Delhi, **Department of Endocrinology & Metabolism, All India Institute of Medical Sciences, *Department of Physical Education, Institute of Home Economics, University of Delhi, New Delhi, India
Table III. Bone mineral density (BMD) parameters of the sports girls and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control girls (n=96)</th>
<th>Sports girls (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body (g/cm²)</td>
<td>1.07 ± 0.087</td>
<td>1.13 ± 0.1*</td>
</tr>
<tr>
<td>Total femur (g/cm²)</td>
<td>0.96 ± 0.12</td>
<td>1.08 ± 0.14*</td>
</tr>
<tr>
<td>Femur neck (g/cm²)</td>
<td>1.07 ± 0.87</td>
<td>1.04 ± 0.13</td>
</tr>
<tr>
<td>33% radius (g/cm²)</td>
<td>0.60 ± 0.09</td>
<td>0.65 ± 0.55*</td>
</tr>
<tr>
<td>Lumbar spine (L1-L4) (g/cm²)</td>
<td>1.07 ± 0.13</td>
<td>1.18 ± 0.14*</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD; *P<0.001 compared to controls.
Comparison of lean mass and its distribution between sportswomen and age matched healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Normal controls N=116</th>
<th>Sports women N=104</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lean mass (Kg)</td>
<td>31.355±3.506</td>
<td>33.667±3.488</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Trunk lean mass (Kg)</td>
<td>14.788±1.663</td>
<td>16.041±1.808</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Leg lean mass (Kg)</td>
<td>10.580±1.391</td>
<td>11.408±1.443</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arm lean mass (Kg)</td>
<td>3.127±0.570</td>
<td>3.326±0.526</td>
<td>0.008</td>
</tr>
<tr>
<td>ASMI (Kg/m²)</td>
<td>5.49±0.62</td>
<td>5.84±0.57</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Normal levels of circulating 25(OH)D?

- Exact cut-offs for “deficiency” and “insufficiency” remain controversial

- Several classifications exist e.g. Lips P:
  - <5 ng/mL - severe hypovitaminosis D
  - 5-10 ng/mL - moderate hypovitaminosis D
  - 10-20 ng/mL - mild hypovitaminosis D
## IOM Recommendations (AI)

<table>
<thead>
<tr>
<th>Age</th>
<th>Children</th>
<th>Men</th>
<th>Women</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth-12 months</td>
<td>400 IU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-18 yrs</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19-50 Yrs</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
</tr>
<tr>
<td>51-70 Yrs</td>
<td>600 IU</td>
<td>600 IU</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>71+</td>
<td>600 IU</td>
<td>600 IU</td>
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</tr>
</tbody>
</table>
Is vitamin D deficiency a major public health issue?
Vitamin D and bone mineral density status of healthy schoolchildren in northern India$^{1,2,3}$

Raman K Marwaha, Nikhil Tandon, Devi Reddy HK Reddy, Rashmi Aggarwal, Rajvir Singh, Ramesh C Sawhney, Bobbin Saluja, M Ashraf Ganie and Satveer Singh

ORIGINAL RESEARCH COMMUNICATION
**Background:** Current data on the prevalence of vitamin D deficiency in India are scarce.

**Objective:** We assessed the calcium-vitamin D-parathyroid hormone axis in apparently healthy children from 2 different socioeconomic backgrounds in New Delhi, India.

**Design:** Clinical evaluation for evidence of vitamin D deficiency was carried out in 5137 apparently healthy schoolchildren, aged 10–18 y, attending lower (LSES) and upper (USES) socioeconomic status schools. Serum calcium, inorganic phosphorus, alkaline phosphatase, 25-hydroxyvitamin D [25(OH)D], and immunoreactive parathyroid hormone were measured in 760 children randomly selected from the larger cohort. Bone mineral density of the forearm and the calcaneum was measured in 555 children by using peripheral dual-energy X-ray absorptiometry.
Vitamin-D Status in Indian Children

- Clinical vitamin D deficiency in 556/5137 (10.82%)
- Genu Varum in 7.5% [B=8%, G=7.2%]
- Genu Valgum in 3.3% [B-2.4%, G-3.9%]
- Low 25(OH)D levels in 84-92%
- 25(OH)D higher in boys than girls
- Mean 25(OH)D values ranged from 11.8±7.2 ng/ml to 12.74±6.17 ng/ml
The present cross-sectional study was conducted to determine the vitamin D status of pregnant Indian women and their breast-fed infants. Subjects were recruited from the Department of Obstetrics, Armed Forces Clinic and Army Hospital (Research and Referral), Delhi. A total of 541 apparently healthy women with uncomplicated, single, intra-uterine gestation reporting in any trimester were consecutively recruited.

Of these 541 women, 299 (first trimester, ninety-seven; second trimester, 125; third trimester, seventy-seven) were recruited in summer (April-October) and 242 (first trimester, fifty-nine, second trimester, ninety-three; third trimester, ninety) were recruited in winter (November-March) to study seasonal variations in vitamin D status.

Clinical, dietary, biochemical and hormonal evaluations for the Ca-vitamin D-parathormone axis were performed. A subset of 342 mother-infant pairs was re-evaluated 6 weeks postpartum.
Vitamin D Status in three trimesters of pregnancy

- Mean serum [25(OH)D]: 9.32±4.89ng/ml
- Hypovitaminosis D: 96.3% subjects (36.8% mild, 41.8% moderate 17.7% severe).
- Trimester Prevalence:
  - summers: 96.9% vs. 92% vs. 98.7%
  - winters: 100% vs. 97.9% vs. 95.6%
- A strong positive correlation was noted in 25(OH)D levels in mother infant pairs (r=0.324, p=0.001)
VITAMIN D STATUS IN INDIAN ADULTS

**Delhi:**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Soldiers Winter</th>
<th>Physicians &amp; Nurses Winter</th>
<th>Physicians &amp; Nurses Summer</th>
<th>Pregnant Women Summer</th>
<th>New Borns Summer</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPTH (pg/ml)</td>
<td>17.6 ±4.8</td>
<td>38.8 ±18.2</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

*Goswami R et al & Marwaha et al  AJCN 2000; 72:472-5*

**Lucknow:**

67% of the subjects had serum 25(OH)D levels < 15 ng/ml

*Arya V, Osteoporosis Int 2004*

**Kashmir Valley:**

Vitamin D deficiency (25 (OH)D<20ng/ml) reported in 83%.
Mild hypovitaminosis D – 25%
Moderate hypovitaminosis D – 33%
Severe hypovitaminosis D – 25%

*Zargar et al Postgraduate Medical Journal 2007*
Tirupati:

- **Mean 25(OH)D values in Males:**
  Urban-18.54±0.8 ng/ml, Rural-23.73±0.8 ng/ml.
- **Mean 25(OH)D values in Females:**
  Urban- 15.5±0.3 ng/ml, Rural- 19±0.89 ng/ml.

  *Harinarayan CV et al: AmJClinNutr 2007*

Delhi Rural:

- Mean vitamin D levels in Females – 10.7 ± 6.3 ng/ml
- Mean Vitamin D levels in Males – 17.68±9.6 ng/ml

  *Goswami R et al JAPI 2008*
VITAMIN D STATUS IN HEALTHY INDIANS AGED 50 YEARS AND ABOVE

Marwaha RK et al JAPI 2013

• Methods:
• Total no. of subjects evaluated: 1346 (Male: 643, Females: 703)
• Mean age: 58 ± 9.5 years (range 50 – 84 years)
• Mean 25(OH)D levels: Males- 9.7±6.8 ng/ml, Females- 9.6±7.51 ng/ml
• Prevalence of Vit D deficiency was noted in 92% subjects.
Vitamin D nutritional status of exclusively breast fed infants and their mothers


BACKGROUND:
Vitamin D nutrition has a profound effect on the development of an infant. Vitamin D status of mothers and their infants are closely correlated. While hypovitaminosis D has emerged as a significant public health problem across all age groups, there is limited information of this condition in lactating mothers and their breast fed infants.

AIM:
To evaluate the vitamin D status of lactating mothers and their breast fed infants.

SUBJECTS AND METHODS:
180 healthy lactating mothers and exclusively breast fed infants, 2-24 weeks old, were recruited for the study. The mother-infant pairs underwent concurrent clinical, biochemical and hormonal evaluation for calcium-vitamin D-PTH axis.
Vitamin-D status in lactating mothers and their exclusively breast fed infants

**Vitamin D status of Lactating mothers:**

- 180 mother-infant pairs from Kalavati hospital were undertaken for the study
- Prevalence of hypovitaminosis D was seen in S: 93.8% [25(OH)D < 20 ng/ml]
- Mean serum 25(OH)D: 10.9±5.8 ng/ml

*Seth A and Marwaha RK et al;JPEM 2009*

**Vitamin D status of Neonates and Infants:**

- Clinical features of vitamin D deficiency: 3.9% (7/180)
- High prevalence of low serum 25(OH)D levels in 80-91% infants 2-24 weeks old.
- Mean 25 (OH)D=11.55±8.3 ng/ml.
- Infants born to mothers with 25(OH)D< 10ng/ml had four times higher risk of developing moderate to severe hypovitaminosis D when compared to those with 25(OH)D levels > 10 ng/ml

*(Seth A & Marwaha RK et al;JPEM 2009,Bhalala et al;Indian Pediatrics)*
Recent studies from across the country clearly reveal a very high prevalence (60%-97%) of vitamin D deficiency in Indians of all age groups and both genders.

It is a major public health problem which needs urgent attention.

Presentation of Vitamin D deficiency:

Symptomatic:  
Rickets in children  
Osteomalacia in adults  
Osteoporosis and Fractures in Elderly  
non-specific symptoms like pain, myalgias  
weakness etc  
Rx: high dose of vitamin D3 followed by maintenance dose.

Asymptomatic/ Non-specific presentation:

Form the bulk of vitamin D deficient subjects in general population
Overcoming Vitamin D deficiency

- Consumption of foods rich in vitamin D
- Sunlight
- Supplementation
- Fortification
Prevalence of low serum 25(OH)D was seen in 90.8% of girls.

Daily intake of Vitamin D through meals was 2-2.5 ug/day (80-100 IU/day) using vitamin D values in foods provided by US food Agricultural Dept.

Significant correlation between serum 25-hydroxyvitamin D and estimated sun exposure (r 0.185, P = 0.001) and percentage body surface area exposed (r 0.146, P = 0.004).

Vitamin D status of apparently healthy schoolgirls from two different socioeconomic strata in Delhi: relation to nutrition and lifestyle.
Conclusion

- In the absence of vitamin D fortification of foods, diet alone appears to have an insignificant role.

- Physical activity and adequate sun exposure are vital for attaining peak bone mass in Indian context.
Food Sources of Vitamin D

- Cod liver oil – 1 TBS
- Salmon 3.5 oz.
- Mackerel 3.5 oz.
- Tuna, canned, in oil, 3 oz.
- Sardines 3.5 oz.
- Milk (fortified) 8 oz.
- Ready to eat cereal (fortified) ¾ - 1 cup
- Egg 1 whole
- Liver, 3.5 oz.
- Cheese, swiss 1 oz.

- 1,360 IU
- 360
- 345
- 200
- 250
- 98
- 40
- 20
- 15
- 12
Dietary advice will not be effective in India:

A) Foods rich in vitamin D are very few

B) Indians being vegetarian by nature, do not consume these foods

It is therefore important that either adequate sun exposure, supplementation or food fortification strategy be adopted to improve vitamin D status of general public.
How much sun exposure?

- What is the best time for sun exposure?
- What % body surface area should be exposed
- Duration of Exposure in winter and summer?

- Vitamin D synthesis depends on:
  - Age
  - Amount of vitamin D obtained from diet
  - Skin pigmentation
  - Sunshine intensity
Regional and seasonal variation of UVB irradiation in different parts of India

Marwaha R K et al, Osteoporosis International, 2015
Figure 1: Hourly Pattern of Mean UVB Index at different geographic locations
Inadequate exposure to sunlight is an important contributing factor for VDD

Significant increase in serum 25(OH)D concentrations is observed with exposure to artificial source ultraviolet B irradiation

Table 2: Changes in biochemical parameters following 4 weeks of sun-exposure in Summer

<table>
<thead>
<tr>
<th></th>
<th>Serum 25 (OH) D (ng/mL)</th>
<th>Calcium (mg%)</th>
<th>ALP (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>$P$ value</td>
</tr>
<tr>
<td>Overall</td>
<td>9.3 ± 5.5</td>
<td>13.3 ± 6.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>n=71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>11.3 ± 4.9</td>
<td>14.6 ± 6.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>n=36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>7.2 ± 5.3</td>
<td>11.9 ± 6.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>n=35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Impact of Solar UVB radiation (290 – 320 nm) on vitamin D synthesis in children with Type IV and V skin in summer


A significant increase in the mean baseline melanin Index was also observed in the study group following sun exposure (forearm: 47.4 ± 5.7 vs. 49.0 ± 5.2, p < 0.001; inner arm: 40.0 ± 5.3 vs. 42.6 ± 5.1, p < 0.001), which was similar in both boys and girls.
Table 4: Change in biochemical parameters among school children with sun exposure in Winter

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>Pre Exposure Winter</th>
<th>Post exposure Winter</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>25(OH)D (ng/ml)</td>
<td></td>
<td>6.3 ± 4.6</td>
<td>5.1 ± 2.7</td>
<td>0.001</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td></td>
<td>82.1 ± 73.2</td>
<td>77.6 ± 68.6</td>
<td>0.20</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td></td>
<td>10.2 ± 0.6</td>
<td>10.0 ± 0.7</td>
<td>0.004</td>
</tr>
<tr>
<td>Phosphate (mg/dl)</td>
<td></td>
<td>4.1 ± 0.7</td>
<td>4.1 ± 0.6</td>
<td>0.74</td>
</tr>
<tr>
<td>ALP (IU/ml)</td>
<td></td>
<td>197.5 ± 93.7</td>
<td>214.7 ± 111.0</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Discussion Cont.

- Estimated average requirement of vitamin D by IOM is 600 IU/day meaning thereby that 600 IU/day are required to maintain baseline levels of serum 25(OH)D (Black LJ et al. 2012; J Nutr; 142: 1102-8).

- Supplementing 100 IU vitamin D will raise serum 25(OH)D levels by 1 ng/ml. (Black LJ et al. 2012; J Nutr; 142: 1102-8).

- Since the increase in serum 25(OH)D following 4 wks of exposure is 3.4-4.9 ng/ml depending on %BSA exposed, it is presumed to be equivalent of supplementing approx. 340 to 490 IU of vitamin D daily.
This additional increase in serum 25(OH)D levels by 3.4 to 4.9 ng/ml in the present study would therefore indicate that approximately 940-1090 IU of vitamin D is being synthesized daily in the skin with 15-30% BSA exposed following 4 wks of sun exposure.

We therefore propose that children with vitamin D deficiency can be supplemented with 4 wkly doses of 60,000 IU cholecalciferol to bring the baseline levels in the range of 20-30 ng/ml and then expose themselves to sunlight everyday for 15-30 minutes with 15-30% BSA during noon time to maintain serum (25OH)D within normal ref range.
Discussion Cont.

• This additional increase in serum 25(OH)D levels by 3.4 to 4.9 ng/ml in the present study would therefore indicate that approximately **940-1090 IU** of vitamin D is being synthesized daily in the skin with 15-30% BSA exposed following 4 wks of sun exposure.

• We therefore propose that children with vitamin D deficiency can be supplemented with 4 wkly doses of 60,000 IU cholecalciferol to bring the baseline levels in the range of 20-30 ng/ml and then expose themselves to sunlight everyday for 15-30 minutes with 15-30% BSA during noon time to maintain serum (25OH)D within normal ref range.
Types of fortification

- **Mass fortification:**
  To fortify foods that are widely consumed by the general population

  Usually mandatory

  Best option when majority of the population has an unacceptable risk, in terms of public health, of becoming deficient in specific micronutrients.
Types of fortification Cont...

- **Target fortification**
  
  Foods aimed at specific population subgroups are fortified eg young children/ elderly, pregnant women
  
  May be mandatory or voluntary

- **Market-driven fortification**
  
  To allow food manufacturers to voluntarily fortify foods available in the market place.
  
  Always voluntary, but governed by regulatory limits
A Randomized Double Blind Controlled Trial to Investigate the Effects of Vitamin D fortified milk on Serum Vitamin D levels in school children, aged 8-12 years
Impact of vitamin D fortified milk supplementation on vitamin D status of healthy school children aged 10–14 years

R. Khadgawat · R. K. Marwaha · M. K. Garg · R. Ramot · A. K. Oberoi · V. Sreenivas · M. Gahlot · N. Mehan · P. Mathur · N. Gupta

- Effects of vitamin D fortification of milk in school children studied

- 713 children randomized into three groups:
  ✓ Group A - 200 mL of unfortified milk per day
  ✓ Group B - 200 mL of milk fortified with 600 IU of vitamin D per day
  ✓ Group C - 200 mL of milk fortified with 1000 IU of vitamin D per day

- Fortification of milk is a safe and effective strategy to deal with widespread vitamin D deficiency

Study subjects (n=482) were divided into three groups receiving 60,000 IU of vitamin D3 weekly for 4, 6 and 8 weeks, respectively, followed by 600 IU daily for 12 weeks.

All three vitamin D loading doses were equally efficacious.

This is an effective strategy for achieving vitamin D sufficiency in Indian adolescents.

Planned Intervention

- **Group A** – no fortification, control group, received 200 ml of unfortified milk daily for 12 weeks
- **Group B** – 200 ml of milk fortified with 600 IU of vitamin D daily for 12 weeks
- **Group C** - 200 ml of milk fortified with 1000 IU of vitamin D daily for 12 weeks

*Randomized by computer generated block randomization plan*
Total no of subjects 796

Number of subjects excluded
10 – Receiving vitamin D supplements
5 – Serum TSH >10 mlU/mL
2 – Type 1 diabetes mellitus
2 – Celiac disease
1 – Receiving antitubercular therapy

Randomization

Group A
Unfortified milk (N = 255)
Could not complete (N = 18)
Subjects analyzed (N = 237)

Group B
Fortified with 600 IU of vitamin D (N = 263)
Could not complete (N = 20)
Subjects analyzed (N = 243)

Group C
Fortified with 1000 IU of vitamin D (N = 258)
Could not complete (N = 25)
Subjects analyzed (N = 233)
### Results: Characteristics of Subjects at Baseline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (No fortification)</th>
<th>Group B (600 IU)</th>
<th>Group C (1000 IU)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>11.74 ± 1.05</td>
<td>11.75 ± 1.08</td>
<td>11.75 ± 1.14</td>
<td>11.75 ± 1.01</td>
</tr>
<tr>
<td>BMI (Kg/meter²)</td>
<td>18.94 ± 3.33</td>
<td>18.84 ± 3.66</td>
<td>18.62 ± 3.50</td>
<td>18.80 ± 3.50</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)</td>
<td>9.8 ± 0.6</td>
<td>9.7 ± 0.7</td>
<td>9.92 ± 0.56</td>
<td>9.8 ± 0.7</td>
</tr>
<tr>
<td>Serum phosphate (mg/dl)</td>
<td>5.06 ± 0.5</td>
<td>5.1 ± 0.5</td>
<td>5.12 ± 0.5</td>
<td>5.09 ± 0.5</td>
</tr>
<tr>
<td>Serum alk phosphatase (IU/L)</td>
<td>270 ± 90</td>
<td>267 ± 82</td>
<td>263 ± 87</td>
<td>267 ± 87</td>
</tr>
<tr>
<td>Urine calcium creatinine ratio</td>
<td>0.04 ± 0.05</td>
<td>0.05 ± 0.07</td>
<td>0.05 ± 0.06</td>
<td>0.05 ± 0.05</td>
</tr>
<tr>
<td><strong>S.25(OH)D (ng/ml)</strong></td>
<td><strong>11.74 ± 5.2</strong></td>
<td><strong>11.4 ± 5.22</strong></td>
<td><strong>11.94 ± 5.63</strong></td>
<td><strong>11.69 ± 5.36</strong></td>
</tr>
<tr>
<td>S.25(OH)D &lt;5 ng/ml (n/%)</td>
<td>19 (8.01%)</td>
<td>23 (9.46%)</td>
<td>17 (7.29%)</td>
<td>39 (8.27%)</td>
</tr>
<tr>
<td>S.25(OH)D 5-&lt;10 ng/ml (n/%)</td>
<td>76 (32.06%)</td>
<td>82 (33.74%)</td>
<td>79 (33.90%)</td>
<td>237 (33.24%)</td>
</tr>
<tr>
<td><strong>S.25(OH)D 10-&lt;20 ng/ml (n/%)</strong></td>
<td><strong>127 (53.58%)</strong></td>
<td><strong>126 (51.85%)</strong></td>
<td><strong>109 (46.78%)</strong></td>
<td><strong>362 (50.77%)</strong></td>
</tr>
<tr>
<td>S.25(OH)D 20-30 ng/ml (n/%)</td>
<td>14 (5.90%)</td>
<td>9 (3.7%)</td>
<td>27 (11.58%)</td>
<td>50 (7.01%)</td>
</tr>
<tr>
<td>S.25(OH)D &gt;30 ng/ml (n/%)</td>
<td>1 (0.42%)</td>
<td>3 (1.23%)</td>
<td>1 (0.42%)</td>
<td>5 (0.7%)</td>
</tr>
</tbody>
</table>

- **Vit D deficiency - 92.3%**
  - Severe 8.27%
  - Moderate 33.24%
  - Mild 50.77%

- **Vitamin D sufficiency (>=30ng/ml) 0.7%**
The mean improvement in serum vitamin D level after fortification

S.25 Vitamin D level

- Control: 11.4 ng/ml
- 600: 22.9 ng/ml
- 1000: 27.6 ng/ml
The % increase in serum 25(OH)D levels following fortification is significantly higher in subjects with very low serum 25(OH)D levels.
# Improvement in Serum vitamin D level after fortification

<table>
<thead>
<tr>
<th></th>
<th>Group A (Control)</th>
<th>Group B (600 IU/D)</th>
<th>Group C (1000 IU/D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>8.01%</td>
<td>6.75%</td>
<td>9.46%</td>
</tr>
<tr>
<td>5-10</td>
<td>32.06%</td>
<td>46.83%</td>
<td>33.74%</td>
</tr>
<tr>
<td>10-20</td>
<td>53.58%</td>
<td>40.5%</td>
<td>51.85%</td>
</tr>
<tr>
<td>20-30</td>
<td>5.90%</td>
<td>4.64%</td>
<td>3.70%</td>
</tr>
<tr>
<td>≥30</td>
<td>0.42%</td>
<td>1.26%</td>
<td>1.23%</td>
</tr>
</tbody>
</table>
Safety of intervention

- Not a single case of hypercalcemia or hypercalciuria as evaluated by serum calcium and Uca/cr ratio was observed in the study.

- No other adverse outcome was observed
Conclusion

We conclude that supplementing milk fortified with vitamin D to children is an effective and safe method of addressing the major public health issue of vitamin D deficiency in children.
Overcoming Vitamin D deficiency

- Sunlight / consumption of foods rich in vitamin D
- Fortification
- Supplementation
124 schoolgirls from lower socioeconomic strata (LSES) and 166 from upper socioeconomic strata (USES) received cholecalciferol granules (60,000 IU) either two-monthly or monthly for one year.

- PTH response was inconsistent.

Oral 60,000 IU vitamin D3 supplement, having different regimen, showed significant increase in serum 25(OH)D levels in vitamin D deficient schoolgirls.

### Effect of vitamin D supplementation on serum 25(OH)D and PTH levels

<table>
<thead>
<tr>
<th></th>
<th>LSES</th>
<th>USES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One-monthly (n=64)</td>
<td>Two-monthly (n=60)</td>
</tr>
<tr>
<td>Serum 25(OH)D (nmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>32.93(1.37)</td>
<td>31.20(1.68)</td>
</tr>
<tr>
<td>6 month</td>
<td>43.90(1.50)</td>
<td>39.53(2.01)</td>
</tr>
<tr>
<td>12 month</td>
<td>59.33(2.64)</td>
<td>53.03(3.05)</td>
</tr>
<tr>
<td>Serum PTH (pg/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>37.64(2.19)</td>
<td>36.41(2.63)</td>
</tr>
<tr>
<td>6 month</td>
<td>30.87(1.82)</td>
<td>29.10(2.35)</td>
</tr>
<tr>
<td>12 month</td>
<td>55.96(3.08)</td>
<td>60.81(4.07)</td>
</tr>
</tbody>
</table>
Baseline: 93.7% school girls were vitamin D deficient

Despite 1 year of supplementation, overall Vitamin D sufficiency was achieved in only 50% of subjects (LSES: 67.8%, USES: 31.9%)

Inability to achieve vitamin D sufficiency in majority of children was probably because of poor absorption due to the fact that fat soluble vitamin D3 was supplemented with water
Objective:
The study aimed to evaluate the efficacy and safety of a single monthly dose of cholecalciferol in healthy school children.

Methods:
• 118 children selected to receive vitamin D supplementation in the form of oral cholecalciferol (60,000 IU) with milk under supervision.
• Serum calcium and 25OHD levels were analyzed from 0 to 12 months.

Results:
• Mean 25OHD levels increased significantly from 12.04±5.27 ng/mL (baseline) to 32.6±7.05 ng/mL (after 12 months) (p < 0.001).
• 96% achieved > 20 ng/dl & 62% achieved >30ng/dl
• None developed hypocalcaemia.

Conclusions:
Vitamin D supplementation (60,000 IU monthly) is reasonable, safe and cost-effective regimen for children to attain and maintain vitamin D sufficiency.
Definition of Miscellization

- Micellization is a new delivery system for fat soluble nutrients that disperse fatty microscopic water-soluble and micellar spheres enabling them to reach the absorptive surface of the intestinal tract, facilitating maximum absorption.

- In the absence of data in humans with regard to efficacy of micellized vitamin D₃, we undertook a small study comparing it’s efficacy vis-a-vis fat soluble vitamin D₃
Total No of Children Recruited : 156 (B-32, G-124)

Group A received fat soluble vitamin D₃ (Calcirol) 60,000 IU/Month for 6 months with milk.

Group B received water miscible vitamin D₃ (DePura), 60,000IU/month for 6 months.

Both groups were given vitamin D₃ under supervision
Results

Baseline Parameters:

- Overall prevalence of vitamin D deficiency: 98.7%
- Severe deficiency (<5 ng/dl) – 80.8%
- Moderate deficiency (5-10 ng/dl) – 7.7%
- Mild deficiency (10-20 ng/dl) – 10.3%
- No difference in mean baseline serum 25(OH)D, PTH between the two groups
## Mean hormonal and biochemical parameters pre and post vitamin D supplementation

<table>
<thead>
<tr>
<th></th>
<th>Overall (n= 156)</th>
<th>Gr. A (N=54) Fat Soluble</th>
<th>Gr. B (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>post</td>
<td>pre</td>
<td>post</td>
</tr>
<tr>
<td><strong>25(OH)D</strong></td>
<td>25.7 ± 3.7</td>
<td>34.5 ± 9.6</td>
<td>5.3 ± 3.4</td>
</tr>
<tr>
<td><strong>PTH</strong></td>
<td>91.8 ± 131</td>
<td>41.2 ± 25.0</td>
<td>77.3 ± 58.0</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td>9.8 ± 0.4</td>
<td>9.8 ± 0.5</td>
<td>9.9 ± 0.4</td>
</tr>
<tr>
<td><strong>Phosphate</strong></td>
<td>4.1 ± 0.4</td>
<td>4.3 ± 0.5</td>
<td>4.1 ± 0.4</td>
</tr>
<tr>
<td><strong>ALP</strong></td>
<td>210.5 ± 123.7</td>
<td>170.1 ± 90.9</td>
<td>141.3 ± 80.5</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Superiority of micellized (water soluble) vitamin D3 over fat soluble vitamin D3

- Mean rise of serum 25(OH)D was $(31.1\, \text{mg/ml})$ in DePura group as against $23.7\, \text{ng/dl}$ in Calcirol group suggesting better absorbption of water soluble vitamin D3 in children.

- The rise in serum 25(OH)D was also significantly higher than that observed by Kuchay et al $(21.1\, \text{ng/dl})$ when they supplemented children with fat soluble Vitamin D3.
100% subjects in Gr. B (DePura) achieved serum 25(OH)D levels of >20ng/dl as against 83.3% in group A (Calcirol).

Furthermore, significantly higher number of subjects from Gr. B (78.4%) achieved >30ng/dl as against 48.2% in Gr. A and 61% in a study by Kuchay et al respectively.
Cont.

- Additional advantages of using micellized form of vitamin D:

  - Can be consumed directly or mixed with food/water/beverages.

  - Allergy: milk/casein, wheat/gluten, eggs, fish, nuts, corn and soya etc
Conclusion

- High prevalence of vitamin D deficiency continues to be present among school children despite creating awareness in public at large for one and half decade.

- Miscible vitamin D₃ is more efficacious than fat soluble vitamin D₃.

- However, more large scale randomized clinical trials in different age groups are required to establish it’s efficacy over fat soluble vitamin D₃.
Impact of three different daily doses of vitamin D3 supplementation in healthy pre-pubertal school girls from North India

Raman Kumar Marwaha, A Mithal, Neetu Bhari, G. Sethuraman, Sushil Gupta, Manoj Shukla, Archana Narang, Aditi Chadda, Nandita Gupta, V Sreenivas, MA Ganie

International Life Sciences Institute (India), Medanta Hospital Gurgaon, Department of Dermatology, All India Institute of Medical Sciences, New Delhi, SGPGI, Lucknow, Uttar Pradesh, Dr. B. R. Sur Homeopathic Medical College, New Delhi, Department of Endocrinology, All India Institute of Medical Sciences, New Delhi, Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India.

Conflict of interest: None
AIM

- Information with regard to daily doses of vitamin D3 supplementation in pre-pubertal children is lacking.

- In view of the above, we undertook this study to evaluate the adequacy and efficacy of daily supplementation of 600IU, 1000IU and 2000IU vitamin D3 in pre-pubertal girls.
Results

• Of 240 recruited girls, 216 completed the study.

• Prevalence of vitamin D deficiency (<20 ng/ml): 100%

• Mild, moderate, and severe deficiency in 44.09%, 52.27% and 3.64% children, respectively.

• Overall increase in serum 25(OH)D following 6 months of supplementation was 19.24 ± 8.18 ng/ml (p<0.01)
Results Cont.

- The increase in the serum 25(OH)D levels was maximum with 2000 IU (24.20 ± 8.28 ng/ml), followed by 1000 IU (17.96±6.55 ng/ml) and 600 IU (15.48±7.00 ng/ml).

- Post-supplementation serum 25(OH)D levels of 20 ng/ml or more were seen in 91% in group A, 97% in group B and 100% group C.
## Table 1: Changes in hormonal parameters following vitamin D supplementation

<table>
<thead>
<tr>
<th></th>
<th>Group A: 600IU (n=74)</th>
<th>Group B: 1000IU (n=67)</th>
<th>Group C: 2000IU (n=75)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum 25(OH)D (ng/ml)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>10.13±3.51</td>
<td>10.21±3.71</td>
<td>9.8±3.73</td>
<td>9.99±3.64</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>25.61±6.29</td>
<td>28.17±6.81</td>
<td>34.00±9.92</td>
<td>29.23±8.00</td>
</tr>
<tr>
<td>Mean change</td>
<td>15.48±7.00</td>
<td>17.96±6.55</td>
<td>24.20±8.28</td>
<td>19.24±8.18</td>
</tr>
<tr>
<td>P value</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
</tr>
<tr>
<td><strong>Serum procollagen type-I N propeptide (PINP) levels (mcg/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>557.44±211.89</td>
<td>508.63±166.52</td>
<td>560.43±218.31</td>
<td>538.9±199.8</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>628.12±180.26</td>
<td>684.16±214.86</td>
<td>664.61±276.13</td>
<td>655.5±218.24</td>
</tr>
<tr>
<td>Mean change</td>
<td>70.68±208.46</td>
<td>175.53±212.36</td>
<td>104.18±253.75</td>
<td>116.6±222.29</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>54.29(59.24-225.15)</td>
<td>158.55(40.99-270.25)</td>
<td>53.10(64.60-216)</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
</tr>
<tr>
<td><strong>Serum C-terminal telopeptide of type I collagen (CTX) levels (mcg/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.856±0.24</td>
<td>0.649±0.18</td>
<td>0.683±0.16</td>
<td>0.745±0.23</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>0.463±0.24</td>
<td>0.348±0.20</td>
<td>0.263±0.14</td>
<td>0.382±0.23</td>
</tr>
<tr>
<td>Mean change</td>
<td>0.393±0.36</td>
<td>0.301±0.21</td>
<td>0.420±0.24</td>
<td>0.363±0.29</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0.375(0.102-0.606)</td>
<td>0.291(0.177-0.470)</td>
<td>0.412(0.270-0.624)</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
<td>p=&lt;0.01</td>
</tr>
</tbody>
</table>
Conclusion

- Supplementation with all three daily doses of vitamin D3 resulted in more than 90% subjects achieving serum 25(OH)D levels of ≥20ng/ml.

- In view of comparable reduction in CTX and increase in PINP and urinary ca²⁺/cr ratio following supplementation in all three groups, it may be safe to assume that 600-1000 IU per day would be adequate daily dose to maintain normal serum 25(OH)D levels of 20ng/ml in pre-pubertal girls.
Definition of Miscellization

- Micellization is a new delivery system for fat soluble nutrients that disperse fatty microscopic water-soluble and micellar spheres enabling them to reach the absorptive surface of the intestinal tract, facilitating maximum absorption.

- In the absence of data in humans with regard to efficacy of micellized vitamin D₃, we undertook a small study comparing its efficacy vis-a-vis fat soluble vitamin D₃.
• Total No of Children Recruited : 156 (B-32, G-124)
• Group A received fat soluble vitamin D3 (Calcirol) 60,000 IU/Month for 6 months with milk.
• Group B received water miscible vitamin D3 (DePura), 60,000IU/month for 6 months.
• Both groups were given vitamin D3 under supervision
Results

Baseline Parameters

- Overall prevalence of vitamin D deficiency: 98.7%
- Severe deficiency (<5 ng/dl) – 80.8%
- Moderate deficiency (5-10 ng/dl) – 7.7%
- Mild deficiency (10-20 ng/dl) – 10.3%
- No difference in mean baseline serum 25(OH)D, PTH between the two groups
Mean hormonal and biochemical parameters pre and post vitamin D supplementation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall (n=156)</th>
<th>Gr. A (N=54)</th>
<th>Gr. B (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pre</td>
<td>post</td>
<td>P-value</td>
</tr>
<tr>
<td>25(OH)D</td>
<td>5.6±3.7</td>
<td>34.5±9.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTH</td>
<td>91.8±131</td>
<td>41.2±25.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.8±0.4</td>
<td>9.8±0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Phosphate</td>
<td>4.1±0.5</td>
<td>4.3±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALP</td>
<td>210.5±123.7</td>
<td>170.1±90.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Superiority of micellized (water soluble) vitamin D3 over fat soluble vitamin D3

- Mean rise of serum 25(OH)D was \(31.1\text{mg/ml}\) in DePura group as against \(23.7\text{ng/dl}\) in Calcirol group suggesting better absorption of water soluble vitamin D3 in children.

- The rise in serum 25(OH)D was also significantly higher than that observed by Kuchay et al \(21.1\text{ng/dl}\) when they supplemented children with fat soluble Vitamin D3.
Cont.

- 100% subjects in Gr. B (DePura) achieved serum 25(OH)D levels of >20ng/dl as against 83.3% in group A (Calcirol).

- Furthermore, significantly higher number of subjects from Gr. B (78.4%) achieved >30ng/dl as against 48.2% in Gr. A and 61% in a study by Kuchay et al respectively.
Cont.

- Additional advantages of using micellized form of vitamin D:
  - Can be consumed directly or mixed with food/water/beverages.
  - Allergy milk/casein, wheat/gluten, eggs, fish, nuts, corn and soya etc
Conclusion

- High prevalence of vitamin D deficiency continues to be present among school children despite creating awareness in public at large for one and half decade.

- Miscible vitamin D3 is more efficacious than fat soluble vitamin D3.

- However, more large scale randomized clinical trials in different age groups are required to establish it’s efficacy over fat soluble vitamin D3.
Supplementation in pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Group A (no vitamin D) (n = 14)</th>
<th>Group B (one dose of 60 000 U vitamin D) (n = 35)</th>
<th>Group C (two doses of 120 000 U vitamin D each) (n = 35)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline 25OHD (nmol/l)</td>
<td>25.8 (18.9–30.7)*</td>
<td>33.4 (22.6–47.7)</td>
<td>40.1 (26.9–58.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>25OHD at delivery (nmol/l)</td>
<td>23.8 (17.2–32.6)</td>
<td>30.9 (24.8–48.1)</td>
<td>53.4 (41.2–88.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum calcium at delivery (mmol/l)</td>
<td>2.31 ± 0.18</td>
<td>2.28 ± 0.27</td>
<td>2.29 ± 0.21</td>
<td>0.41</td>
</tr>
<tr>
<td>Increment of 25OHD (nmol/l)</td>
<td>0.4 (-6.5–16.8)</td>
<td>-2.1 (-10.7–13.1)</td>
<td>13.4 (0.2–42.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>25OHD &gt;80 nmol/l at delivery (nmol/l)</td>
<td>1/14 (7%)</td>
<td>2/35 (5.7%)</td>
<td>12/35 (34.2%)</td>
<td>0.003</td>
</tr>
<tr>
<td>25OHD at delivery conducted in winter (nmol/l)</td>
<td>14.9 (n = 1)</td>
<td>26.9 (22.9–33.3) (n = 11)</td>
<td>43.7 (35.3–62.0)</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>25OHD &gt;80 nmol/l at delivery in winter</td>
<td>0/1</td>
<td>0/11</td>
<td>3/14 (21%)</td>
<td>0.23*</td>
</tr>
</tbody>
</table>

**Anthropometric indices:** Differences persisted at 9 months

- **Head circumference**
  - Group A: 33.6 ± 0.8
  - Group B: 34.4 ± 0.6
  - Group C: 34.5 ± 0.9

- **Length**
  - Group A: 49.4 ± 2.4
  - Group B: 50.1 ± 0.9
  - Group C: 50.3 ± 0.9

- **Weight (kg)**
  - Group A: 2.8 ± 0.4
  - Group B: 3.0 ± 0.4
  - Group C: 3.1 ± 0.4

*Sahu et al, EJCN, 2009*
Words of Wisdom

- The richest wealth is Wisdom
- The strongest weapon is Patience.
- The best security is Faith.
- The greatest tonic is Laughter.
- Surprisingly all are free and so is Wonder Vitamin D
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