Vitamin D
Vitamin D

- Vitamin D insufficiency is an emerging global health concern
- There is a worldwide epidemic of vitamin D deficiency in various populations such as:
  - Infants
  - Pregnant and lactating women
  - Elderly
  - Individuals living in latitudes far from the equator
  - Persons who avoid the sun or ultraviolet radiation in the blue spectrum (UVB)
  - Populations with dark skin pigmentation
Vitamin D

- Vitamin D is a steroid which, in its active form, has a hormone activity

- The major sources of vitamin D in humans are cutaneous synthesis, diet, and supplements

- Scientific evidence indicates that Vitamin D has a new and more critical role as a ubiquitous hormone at the centre of a complex endocrine, paracrine, and autocrine system involved in maintaining general health
Vitamin D

- Literature points out that adequate vitamin D status is important for optimal function of many organs and tissues throughout the body.

<table>
<thead>
<tr>
<th>Serum 25-Hydroxyvitamin D (ng/ml)</th>
<th>Vitamin D Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10</td>
<td>Severe deficiency</td>
</tr>
<tr>
<td>10-20</td>
<td>Deficiency</td>
</tr>
<tr>
<td>21-29</td>
<td>Insufficiency</td>
</tr>
<tr>
<td>≥30</td>
<td>Sufficiency</td>
</tr>
<tr>
<td>&gt;150</td>
<td>Toxicity</td>
</tr>
</tbody>
</table>

JH Lee et al. Vitamin D Deficiency and CV Risk. 2008. JACC;52(24):1949-56
**Why D3 for knowing the status?**

25(OH)D is major circulating form of vitamin D, with a circulating half-life of approximately 2–3 wk

1,25(OH)$_2$D has a circulating half-life of approximately 4 h

1,25(OH)$_2$D circulates at 1000 times lower concentration than 25(OH)D, and the blood level is tightly regulated by serum levels of PTH, calcium, and phosphate
Why D3 for knowing the status?

Serum 1,25(OH)$_2$D does not reflect vitamin D reserves, and measurement of 1,25(OH)$_2$D is not useful for monitoring vitamin D status of patients.

Serum 1,25(OH)$_2$D is frequently either normal or even elevated in those with vitamin D deficiency, due to secondary hyperparathyroidism and thus 1,25(OH)$_2$D measurement does not reflect vitamin D status.
Risk factors for Vit D deficiency

- Elderly
- Darkly pigmented skin
- Institutionalized or homebound
- Increased distance from the equator
- Winter season
- Covered-up clothing and/or usage of sunscreen
- Air pollution

- Smoking
- Obesity
- Malabsorption
- Liver disease
- Renal disease
- Certain medications like anticonvulsants, glucocorticoids, Immunosuppressants, anti retroviral therapy etc.

JH Lee et al. Vitamin D Deficiency and CV Risk. 2008. JACC;52(24):1949-56
Vit D receptor (VDR)

- Nuclear receptor found in most organs
- Activated by physiologically active form of vitamin D: 1,25-(OH)\(_2\)-D
- Calciotropic actions of 1,25-(OH)\(_2\)-D include enhancement of intestinal calcium and phosphorus absorption, suppression of parathyroid hormone secretion and stimulation of bone resorption
- Wide tissue distribution of VDR led to recognition of noncalciotropic actions of 1,25-(OH)\(_2\)-D
Role of Vit D

- Vitamin D has a key role in calcium and phosphate balance and bone structure.

- Most tissues and cells in the body have a vitamin D receptor -
  - Several of these cells possess required enzymes to convert the primary circulating form of vitamin D to the active form.
Role of Vit D.

- Vitamin D plays an interesting role in decreasing risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease.

- Ecological and observational studies show associations between low concentration of serum 25-hydroxyvitamin D (25[OH]D) and increased risk of cancer, cardiovascular diseases, disorders of glucose metabolism, neurodegenerative diseases and death.
Vitamin D and Bone
Vitamin D

plays an important role in maintaining adequate levels of serum calcium and phosphorus
Traditionally, vitamin D has been associated with bone health.

Vitamin D deficiency leads to:
- Rickets and growth retardation in children
- Osteomalacia, osteoporosis and increased risk of fractures in adults
Symptomatic Evaluation

- Muscle pain
- Muscle cramps
- Joint pain
- Fatigue
- Headaches
- Constipation
- Restless sleep
- Poor concentration
Vitamin D Status in India – Its Implications and Remedial Measures

CV Harinarayan*, Shashank R Joshi**
<table>
<thead>
<tr>
<th>LAT</th>
<th>LONG</th>
<th>Location</th>
<th>n</th>
<th>STUDY POPULATION</th>
<th>AGE (Yrs)</th>
<th>25 OH D</th>
<th>UNIT</th>
<th>Ref No</th>
</tr>
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<tbody>
<tr>
<td>34.6° N</td>
<td>74.48° E</td>
<td>Kashmir</td>
<td>64</td>
<td>Men</td>
<td>28.8 ± 4.9</td>
<td>37.7 ± 30</td>
<td>nmol/l</td>
<td>Zargar et al.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valley</td>
<td>28</td>
<td>Women</td>
<td>26.8 ± 4.8</td>
<td>13.8 ± 11</td>
<td>nmol/l</td>
<td></td>
</tr>
<tr>
<td>30.3° N</td>
<td>76.47° E</td>
<td>Chandigarh</td>
<td>329</td>
<td>Males and females (summer)</td>
<td>19.4 ± 1.48</td>
<td>52.9 ± 33.7</td>
<td>nmol/l</td>
<td>Santosh et al.29</td>
</tr>
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<td>237</td>
<td>Males and females (winter)</td>
<td>19.4 ± 1.43</td>
<td>31.8 ± 21.1</td>
<td>nmol/l</td>
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<td>28.35° N</td>
<td>77.12° E</td>
<td>Delhi</td>
<td>12</td>
<td>Controls (Resident Doctors)</td>
<td>25–35</td>
<td>8.3 ± 2.5</td>
<td>µg/ml</td>
<td>Harinarayan et al.30</td>
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<td>Pregnant women (summer)</td>
<td>23 ± 3</td>
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<td>nmol/l</td>
<td>Goswami et al.31</td>
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<td>Newborn (summer)</td>
<td>newborn</td>
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<td>Soldiers males (winter)</td>
<td>21.2 ± 2</td>
<td>41.17 ± 11.73</td>
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<td>19</td>
<td>Phys. and nurse (summer)</td>
<td>23 ± 5</td>
<td>7.89 ± 3.49</td>
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<td></td>
<td>19</td>
<td>Phys. and nurse (winter)</td>
<td>24 ± 4</td>
<td>17.97 ± 7.98</td>
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<td></td>
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<td>15</td>
<td>Depigmented persons (winter)</td>
<td>43 ± 16</td>
<td>18.2 ± 11.23</td>
<td>nmol/l</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td>Delhi</td>
<td>26</td>
<td>Toddlers (Mori gate)</td>
<td>16 ± 4 mo</td>
<td>12.4 ± 7</td>
<td>ng/ml</td>
<td>Agarwal et al.30</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Infants (Gurgaon)</td>
<td>16 ± 4 mo</td>
<td>28 ± 7</td>
<td>ng/ml</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Delhi</td>
<td>47</td>
<td>Sunder Nagar Jan 2001</td>
<td>9–30 mo</td>
<td>96 ± 25.7</td>
<td>nmol/l</td>
<td>Tiwari et al.32</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>49</td>
<td>Rajiv colony Feb 2001</td>
<td>9–30 mo</td>
<td>23.8 ± 27</td>
<td>nmol/l</td>
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<td>48</td>
<td>Rajiv Colony Aug 2001</td>
<td>9–30 mo</td>
<td>17.8 ± 22.4</td>
<td>nmol/l</td>
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<td>52</td>
<td>Gurgaon Aug 2001</td>
<td>9–30 mo</td>
<td>19 ± 20</td>
<td>nmol/l</td>
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<td>193</td>
<td>LSES School girls</td>
<td>12.4 ± 3.2</td>
<td>34.6 ± 17.43</td>
<td>nmol/l</td>
<td>Puri et al.33</td>
</tr>
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<td></td>
<td>211</td>
<td>USES School girls</td>
<td>12.3 ± 3</td>
<td>29.4 ± 12.7</td>
<td>nmol/l</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delhi</td>
<td>42</td>
<td>LSES School boys</td>
<td>10–12</td>
<td>12.4 ± 5.5</td>
<td>ng/ml</td>
<td>Marwaha et al.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>85</td>
<td>USES School boys</td>
<td>13–15</td>
<td>11.3 ± 5.8</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>40</td>
<td>USES School boys</td>
<td>16–18</td>
<td>11.3 ± 5.3</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>33</td>
<td>USES School boys</td>
<td>10–12</td>
<td>19.3 ± 8.8</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td>70</td>
<td>USES School boys</td>
<td>13–15</td>
<td>13.1 ± 7</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
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<td>55</td>
<td>USES School girls</td>
<td>16–18</td>
<td>13.5 ± 7</td>
<td>ng/ml</td>
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<td>78</td>
<td>USES School girls</td>
<td>10–12</td>
<td>11 ± 6.5</td>
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<td>Delhi</td>
<td>123</td>
<td>LSES School girls</td>
<td>13–15</td>
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<td>62</td>
<td>USES School girls</td>
<td>16–18</td>
<td>11 ± 5.7</td>
<td>ng/ml</td>
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<tr>
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<td>Delhi</td>
<td>47</td>
<td>LSES School girls</td>
<td>10–12</td>
<td>12.5 ± 8.9</td>
<td>ng/ml</td>
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<tr>
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<td></td>
<td></td>
<td>62</td>
<td>LSES School girls</td>
<td>13–15</td>
<td>10.2 ± 5.7</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delhi</td>
<td>63</td>
<td>LSES School girls</td>
<td>16–18</td>
<td>12.9 ± 10.5</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delhi</td>
<td>40</td>
<td>Indian Paramilitary forces men</td>
<td>20–30</td>
<td>18.4 ± 5.3</td>
<td>ng/ml</td>
<td>Tandon N et al.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>Indian Paramilitary forces women</td>
<td>20–30</td>
<td>25.3 ± 7.4</td>
<td>ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delhi</td>
<td>32</td>
<td>Rural males</td>
<td>42.8 ± 16.6</td>
<td>44.2 ± 24.4</td>
<td>nmol/l</td>
<td>Goswami et al.36</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Rural females</td>
<td>43.4 ± 12.6</td>
<td>26.9 ± 15.9</td>
<td>nmol/l</td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± SEM; **Values are median and inter-quartile range; For conversion from nmol to ng—multiply by 0.4; Age Adj. Age Adjusted; LAT, Latitude; LONG, Longitude.
<table>
<thead>
<tr>
<th>Delhi</th>
<th>Mothers</th>
<th>NA</th>
<th>9.8</th>
<th>ng/ml</th>
<th>Jain et al.**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>97</td>
<td>Mothers 1st Trimester (summer)</td>
<td>24.4 ± 2.67</td>
<td>23.4 ± 11.3</td>
<td>mmol/l</td>
</tr>
<tr>
<td></td>
<td>59</td>
<td>Mothers 1st Trimester (winter)</td>
<td>25.7 ± 9.2</td>
<td>19.6 ± 9.2</td>
<td>mmol/l</td>
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<tr>
<td></td>
<td>125</td>
<td>Mothers 2nd Trimester (summer)</td>
<td>25.2 ± 2.94</td>
<td>25.7 ± 15.1</td>
<td>mmol/l</td>
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<td>93</td>
<td>Mothers 2nd Trimester (winter)</td>
<td>20.2 ± 10.6</td>
<td>20.2 ± 10.6</td>
<td>mmol/l</td>
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<td>77</td>
<td>Mothers 3rd Trimester (summer)</td>
<td>24.26 ± 2.82</td>
<td>27.7 ± 9.2</td>
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<td>90</td>
<td>Mothers 3rd Trimester (winter)</td>
<td>21.1 ± 12.4</td>
<td>21.1 ± 12.4</td>
<td>mmol/l</td>
</tr>
<tr>
<td>subset</td>
<td></td>
<td>Mothers 6 wks postpartum</td>
<td>19.6 ± 8.3</td>
<td>19.6 ± 8.3</td>
<td>mmol/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infants</td>
<td>6 weeks</td>
<td>22.3 ± 10.5</td>
<td>mmol/l</td>
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<tr>
<td>Delhi</td>
<td>703</td>
<td>Women</td>
<td>50 ± 9.5</td>
<td>9.78 ± 8.3</td>
<td>mmol/l</td>
</tr>
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<td>643</td>
<td>Males</td>
<td>50 ± 9.5</td>
<td>9.81 ± 6.79</td>
<td>mmol/l</td>
</tr>
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<td></td>
</tr>
<tr>
<td>26.55° N 80.59° E</td>
<td>Lucknow</td>
<td>140</td>
<td>Pregnant women (urban)</td>
<td>24 ± 4.1</td>
<td>14 ± 9.5</td>
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<td></td>
<td>67</td>
<td>Pregnant women (rural)</td>
<td>24.7 ± 5.1</td>
<td>14 ± 9</td>
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<td></td>
<td>29</td>
<td>Cord Blood (OSM)</td>
<td>-</td>
<td>12 ± 8</td>
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<tr>
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<td>178</td>
<td>Cord Blood (no OSM)</td>
<td>-</td>
<td>14.3 ± 9.5</td>
</tr>
<tr>
<td>Lucknow</td>
<td>139</td>
<td>Pregnant women (summer)</td>
<td>Age Adj u</td>
<td>55.5 ± 19.8</td>
<td>mmol/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>139</td>
<td>Pregnant women (winter)</td>
<td>Age Adj u</td>
<td>27.3 ± 12.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>28</td>
<td>Girls (winter)</td>
<td>Age Adj u</td>
<td>31.3 ± 1.5</td>
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<tr>
<td></td>
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<td>34</td>
<td>Boys (winter)</td>
<td>Age Adj u</td>
<td>67.5 ± 29</td>
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<tr>
<td>Lucknow</td>
<td>53</td>
<td>Controls</td>
<td>61 ± 36</td>
<td>61 ± 36</td>
<td>mmol/l</td>
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<tr>
<td></td>
<td>40</td>
<td>Rickets/OSM</td>
<td>49 ± 38</td>
<td>49 ± 38</td>
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<td>Lucknow</td>
<td>92</td>
<td>Healthy volunteers</td>
<td>34.2 ± 6.7</td>
<td>12.3 ± 11</td>
<td>ng/ml</td>
</tr>
<tr>
<td>18.56° N 72.54° E</td>
<td>Mumbai</td>
<td>42</td>
<td>Mothers Suppl Ca 250–500 additinal</td>
<td>20 to 35</td>
<td>23 ± 11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42</td>
<td>Cord Blood</td>
<td>-</td>
<td>19.5 ± 9.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35</td>
<td>Infants</td>
<td>3 mo</td>
<td>18.2 ± 9.8</td>
</tr>
<tr>
<td>Mumbai</td>
<td>558</td>
<td>Males</td>
<td>30.1 ± 3.53</td>
<td>18.9 ± 8.9</td>
<td>ng/ml</td>
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<td>579</td>
<td>Females</td>
<td>30.52 ± 3.57</td>
<td>15.8 ± 9.1</td>
<td>ng/ml</td>
</tr>
<tr>
<td>18.31° N 73.55° E</td>
<td>Pune</td>
<td>25</td>
<td>Male toddlers (outdoor)</td>
<td>2.26 ± 0.8</td>
<td>95.96 (91.6)</td>
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<tr>
<td></td>
<td></td>
<td>25</td>
<td>Female toddlers (outdoor)</td>
<td>2.53 ± 0.8</td>
<td>130.2(67.7)**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31</td>
<td>Male toddlers (indoor)</td>
<td>2.94 ± 0.6</td>
<td>14.0 (32.0)**</td>
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<td></td>
<td></td>
<td>29</td>
<td>Female toddlers (indoor)</td>
<td>2.70 ± 0.6</td>
<td>5.2 (21.1)**</td>
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<td>13.62° N 79.4° E</td>
<td>Tirupati</td>
<td>191</td>
<td>Tirupati rural*</td>
<td>44 ± 1.03</td>
<td>21 ± 0.46</td>
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</tbody>
</table>

**Mean ± SEM; **Values are median and inter-quartile range; For conversion from nmol to ng—multiply by 0.4; Age Adj u, Age Adjusted; LAT, Latitude; LONG, Longitude.
**Table 1. Vitamin D status of India summarized based on latitude and longitude**

<table>
<thead>
<tr>
<th>Location</th>
<th>Gender</th>
<th>Vitamin D Level Mean ± SEM (ng/ml)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tirupati</td>
<td>Urban men*</td>
<td>47 ± 1.5</td>
<td>Harinarayan et al.848</td>
</tr>
<tr>
<td>Tirupati</td>
<td>Rural men*</td>
<td>45 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Urban women*</td>
<td>46 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Rural women*</td>
<td>41 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Urban children male*</td>
<td>11 ± 1</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Rural children male*</td>
<td>12 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Urban children female*</td>
<td>13.5 ± 0.6</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Rural children female*</td>
<td>12.6 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Tirupati</td>
<td>Post menopausal</td>
<td>54 ± 8</td>
<td>Harinarayan et al.99</td>
</tr>
<tr>
<td>Tirupati</td>
<td>Women in reproductive age group*</td>
<td>37.5 ± 0.94</td>
<td>Harinarayan et al.20</td>
</tr>
<tr>
<td>Tirupati</td>
<td>Post menopausal*</td>
<td>53.3 ± 0.72</td>
<td></td>
</tr>
<tr>
<td>Bangalore</td>
<td>Males*</td>
<td>50 ± 1.44</td>
<td>Harinarayan et al.51</td>
</tr>
<tr>
<td>Vellore</td>
<td>Females*</td>
<td>51 ± 0.6</td>
<td>Paul et al.52</td>
</tr>
<tr>
<td>12.58° N 77.38° E</td>
<td>Post menopausal women</td>
<td>60.1 ± 5</td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± SEM; **Values are median and inter-quartile range; For conversion from nmol to ng—multiply by 0.4; Age Adj, Age Adjusted; LAT, Latitude; LONG, Longitude.
SUMMARY OF INDIAN STUDIES

• All studies uniformly point to low 25(OH)D levels in the populations studies despite abundant sunshine in our country.

• All studies have uniformly documented low dietary calcium intake compared to Recommended Daily/Dietary Allowances (RDA) by Indian Council of Medical Research (ICMR).

• The vitamin D status of children is very low in both urban and rural population studied.

• In some of the studies it has been clearly shown that the 25(OH)D levels were directly proportional to the duration of exposure to sunlight. This is evident from the vitamin D status of rural population who were agricultural workers and had their chest and tarso exposed to sunlight compared to the urban population who were white collared workers. Hence exposure to sunlight has positive effect on the vitamin D status of individuals.

CV Harinarayan, Shashank R Joshi. Vitamin D Status in India – Its Implications and Remedial Measures. JAPI 2009,57:40-48
Figure 7. (A) Graph showing the inverse correlation between the 25 (OH) D levels and latitude (r = -0.48; p < 0.0001) from various studies conducted in the country (Table 1). (B) The 25 (OH) D levels of various studies from India along with latitude and location from various studies conducted in the country (Table 1).
SUMMARY OF INDIAN STUDIES

• Pregnant women and their new born had low vitamin D status.

• Residents of northern tip of India in Kashmir valley had low 25(OH)D levels.

• Indian paramilitary forces who had dietary calcium well above the RDA and daily exercises in sunlight in the morning hours had better 25(OH)D levels compared to the civilian counterparts.

• Dietary calcium supplementation had positive effect on 25(OH)D levels.
The prevalence of “sub-clinical 25(OH)D deficiency (hypovitaminosis D)” may be over looked due to vague clinical presentation.

Vitamin D supplementation has to be considered in patients with osteoporosis (Keeping in mind the hypovitaminosis D in majority of the population).

Food fortification programs have to be thought of in various parts of the country depending on their vitamin D status and dietary calcium intake.

The Bone Mineral Density (BMD) measured in these populations could be incorrect. Early osteomalacia could co-exist with osteoporosis in the elderly population and can give fallacious BMD values misleading the diagnosis.
The clinical presentation of various diseases is modified. Early osteomalacia can coexist with osteoporosis.

• Clinical presentation of primary hyperparathyroidism is altered (the clinical presentation is that of bone disease and the adenomas are large).

• Patients with primary hyperparathyroidism require vitamin D and calcium supplementation to prevent “Hungry bone syndrome” in the post operative period.

CV Harinarayan, Shashank R Joshi. Vitamin D Status in India – Its Implications and Remedial Measures. JAPI 2009,57:40-48
Vitamin D status and sun exposure in India

Chittari V. Harinarayan,1,* Michael F. Holick,2 Upadrasta V. Prasad,1 Palavali S. Vani1 and Gutha Himabindu1

1Department of Endocrinology and Metabolism; Sri Venkateswara Institute of Medical Sciences; Tirupati; Andhra Pradesh, India; 2Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes Vitamin D; Skin and Bone Research Laboratory; Boston University Medical Center; Boston University School of Medicine; Boston, MA USA

Background: Little if any cutaneous production of vitamin D3 occurs at latitudes above and below 35° N and 35° S during the winter months. It was postulated that those residing in tropics synthesize enough vitamin D3 year round. Several studies have documented the effect of latitude, season and time of the day on the cutaneous production of vitamin D3 in an ampoule model. Studies from India have shown high prevalence of vitamin D deficiency despite abundant sunshine.

Results: The percent conversion of 7-DHC to previtamin D3 and its photoproducts and formation of previtamin D3 and vitamin D3 was maximal between 11 a.m. to 2 p.m. of the day during the entire year (median 11.5% and 10.2% respectively at 12.30 p.m.).

Methods: We studied the influence of season and time of the day on synthesis of previtamin D3 in an ampoule model in Tirupati, (latitude 13.40° N and longitude 77.2° E) south India, between May 2007 to August 2008. Sealed borosilicate glass ampoules containing 50 μg of 7-DHC in 1 ml of methanol were exposed to sunlight hourly from 8 a.m. until 4 p.m. The percent conversion of 7-DHC to previtamin D3 and its photoproducts and the percent of previtamin D3 and vitamin D3 formed was estimated and related to solar zenith angle.

Conclusions: Therefore at this latitude exposure to sunlight between the hours of 11 a.m. and 2 p.m. will promote vitamin D production in the skin year round.
Vitamin D status and sun exposure in India

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1Department of Endocrinology and Metabolism; Sri Venkateswara Institute of Medical Sciences; Tirupati; Andhra Pradesh, India; 2Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes Vitamin D; Skin and Bone Research Laboratory; Boston University Medical Center; Boston University School of Medicine; Boston, MA USA

Figure 2. Showing the mean ± SD of the zenith angles, percent conversion of 7-Dehydrocholesterol (7-DHC) to previtamin D₃, and photoproducts, and the percentage of previtamin D₃ and vitamin D₃ against time (for the study duration).
ROLE OF VITAMIN D:
BEYOND BONE
Vitamin D Deficiency

Osteoporosis/Osteopenia
Fracture

Myopathy/Muscular Pain

Cancer

Neurological Disorders

Respiratory Infections

Autoimmune Diseases (Rheumatoid arthritis)

Diabetes

Cardiovascular problems/Hypertension

Autoimmune Diseases
(Rheumatoid arthritis)

Neurological Disorders

Vitamin D Deficiency

Cancer

Diabetes

Cardiovascular problems/Hypertension

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Cancer
Focus on usage in:

Diabetes
Hypertension
Influenza
Asthma
Vit D and DM
Type 2 DM

- For glucose intolerance and T2DM to develop, following has to be present:
  - Defects in pancreatic beta-cell function
  - Insulin sensitivity
  - Systemic inflammation
Vit D and Insulin secretion

- Insulin secretion is a calcium dependent process
  - Alterations in calcium flux can have adverse effects on beta cell secretory function

- Vitamin D regulates extracellular calcium and calcium flux through the beta cell

- Vitamin D insufficiency alter balance between extracellular and intracellular beta cell calcium pools
  - Normal insulin release interfered
Calcium is essential for insulin-mediated intracellular processes in insulin-responsive tissues such as skeletal muscle and adipose tissue.

Changes in intracellular cytosolic calcium contribute to peripheral insulin resistance:
- impaired insulin signal transduction leading to decreased GLUT-4 activity.
Vit D and Insulin resistance...

Vitamin D has a beneficial effect on insulin action either by

- Stimulating expression of insulin receptor
- Regulating extracellular calcium
  - Ensures normal calcium influx through cell membranes and adequate intracellular cytosolic calcium
Vit D and Inflammation

- T2DM is associated with systemic inflammation

- Systemic inflammation linked to
  - Insulin resistance
  - Beta cell dysfunction due to elevated cytokines triggering beta cell apoptosis
Vit D and Inflammation

- Vitamin D modulates generation and effects of cytokines

Improves insulin sensitivity
Promotes beta cell survival

LADA and Vit D
(Latent Autoimmune Diabetes in Adults)
Vit D and LADA

Latent autoimmune diabetes in adults (LADA) is a type 1 diabetes which shows slow progression to insulin dependence

Studies show that Vit D + Insulin:

- *Protect pancreatic beta cells*
- *Maintain natural insulin production better than insulin alone*

IMPROVEMENT IN PANCREATIC $\beta$-CELL FUNCTION WITH VITAMIN D AND CALCIUM SUPPLEMENTATION IN VITAMIN D-DEFICIENT NONDIABETIC SUBJECTS

Chittari Venkata Harinarayan, MD, DM, FAMS, FRCP (Glasgow), FRCP (Edin)$^1$; Shalini Arvind, MSc$^2$; Shalini Joshi, MD, ABIM$^3$; Kandavel Thennarasu, PhD$^4$; Vasanthi Vedavyas, MSc, RD$^2$; Anushka Baindur, MSc, RD$^2$

**Objective:** The objective was to examine the effect of vitamin D and calcium supplementation on $\beta$-cell function and plasma glucose levels in subjects with vitamin D deficiency.

**Conclusion:** Optimizing serum 25-OHD concentrations and supplementation with calcium improves fasting plasma glucose levels and $\beta$-cell secretory reserve. Larger randomized control studies are needed to determine if correction of 25-OHD deficiency will improve insulin secretion and prevent abnormalities of glucose homeostasis.

http://www.endocrinepractice.org/home/main.mpx
Vit D and Hypertension
Vit D and Hypertension

- Renin angiotensin system (RAS) is a regulatory cascade that plays a critical role in the regulation of blood pressure, electrolyte, and plasma volume homeostasis.

- Inappropriate stimulation of the RAS is associated with hypertension.

- Vitamin D is a potent endocrine suppressor of renin biosynthesis thereby regulating the RAS.
**Vit D and Hypertension**

- Low Vit D status associated with secondary elevation of PTH as well as increased arterial resistance leading to hypertension

- Elevated PTH associated with
  - Increased renin expression and activation of RAS system
  - Upregulates sympathetic nervous system activity
Vit D and Hypertension

- Randomized, placebo-controlled study in elderly women

Results showed that

- 800 IU of vitamin D₃ + 1200 mg of calcium significantly reduced blood pressure by 9.3% after 8 weeks

- 1200 mg of calcium alone reduced blood pressure by only 4.0% ($P = .02$)
148 women, aged 74 ± 1
DB-RCT
baseline 25(OH)D < 50 nmol/L
treated for 8 wks with:
Ca 1200 mg/d or
Ca + 800 IU vit D/d

*Sfeifer et al., JCEM 2001; 86:1633–37*
Vit D and Hypertension

- Two prospective cohort studies with measured 25(OH)D levels were followed for 4 to 8 years
  - 613 men from the Health Professionals' Follow-Up Study
  - 1198 women from the Nurses' Health Study

- During 4 years of follow-up, multivariable pooled relative risk of incident hypertension among those whose measured plasma 25(OH)D levels were <15 ng/mL (ie, vitamin D deficiency) compared with those whose levels were ≥30 ng/mL using the random-effects model was 3.18

- **Conclusion:** Plasma 25(OH)D levels are inversely associated with risk of incident hypertension
- 1811 men & women with measured 25(OH)D levels**
- 4 yrs’ observation
- 97 cases of incident hypertension
- RR computed for 25(OH)D <15ng/mL vs. >30 ng/mL

*Forman at al., 2007; Hypertension 49:1063
**Health Profs Follow-up Study & Nurses Health Study
Vit D and Influenza
Vit D and Influenza

- Vitamin D stimulates genetic expression of antimicrobial peptides, which have broad-spectrum antimicrobial activity and inactivate influenza virus

- Vitamin D promotes lysosomal enzyme acid phosphatase and secretion of $H_2O_2$

- In the macrophage, presence of vitamin D suppresses pro-inflammatory cytokines like Interferon $\gamma$, TNF$\alpha$, and IL-12 and dampen the signs and symptoms of acute inflammation

Vit D and Influenza

• The 104 subjects in the placebo group (light shade) reported cold and flu symptoms year around with the most symptoms in the winter.

• While on 800 IU per day (intermediate shade) the 104 test subjects were as likely to get sick in the summer as the winter.

• Only one of the 104 test subjects had cold/influenza symptoms during the final year of the trial, when they took 2,000 IU of vitamin D per day (dark shading).

Vit D and Influenza

- Prospective cohort study done to determine if serum 25 hydroxyvitamin D concentrations correlated with the incidence of acute viral respiratory tract infections
- One hundred ninety-five (98.5%) of the enrolled participants completed the study
- Vit D$_3$ concentrations of 38 ng/ml or more was associated with a significant (p<0.0001) two-fold reduction in risk of developing acute respiratory tract infections and with a marked reduction in the percentages of days ill

Vit D and Influenza

- Randomized, double-blind, placebo-controlled trial comparing vitamin D$_3$ supplements (1200 IU/d) with placebo in schoolchildren

- Primary outcome was incidence of influenza A and Secondary outcome was asthma attacks in asthmatic children

- Vit D$_3$ supplementation associated with lesser incidences of influenza and asthmatic attacks in asthmatic children

Am J Clin Nutr 2010;91:1255–60
Vit D and Asthma
Vit D and Asthma

- Vitamin D modulates the macrophage response, preventing the release of excessive inflammatory cytokines and chemokines

Inflammatory cytokine expression [e.g. interleukin (IL)-1α, IL-1β, tumour necrosis factor (TNF)-α] inhibited

Vitamin D inhibits IL-12 by interfering NF-KB pathway

Vit D and Asthma...

IL-12 stimulates development of T helper type 1 (Th1) lymphocytes and inhibits the development of Th2 lymphocytes.

Vitamin D reduces transcription of Th1 cytokines such as IL-2, granulocyte–macrophage colony-stimulating factor (GM–CSF) and interferon (IFN)-γ.

Increased expression of anti-inflammatory Th2 cytokines IL-4, -5, -10.

Vitamin D and its various actions in the immune system. (A) Vitamin D inhibits the production and proliferation of Th1 and Th0 cells by inhibiting IL-2, IFNγ, and TNFα; vitamin D promotes the production of Treg cells by facilitating production of IL-10. (B) Vitamin D promotes a Th2-mediated immune response profile by promoting IL-4, IL-5, and IL-10. Vitamin D inhibits a Th17-mediated immune response profile (and thus inhibits IL-17) by inhibiting IL-6 and IL-23. (C) Vitamin D inhibits the production of B-cells, the differentiation of B-cells into plasma cells, and the production of antibodies by B-cells. (D) Vitamin D promotes nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, α in respiratory epithelial cells, which inhibits NF-κB, in turn promoting antiviral and immunomodulatory interferon signaling. Th, T helper cell; Treg, T regulatory cell.
Vit D and Asthma

- Administration of Vitamin D to glucocorticoid-resistant asthmatic patients enhance responsiveness by restoring defective IL-10 response to glucocorticoids by CD4+ T cells in these individuals

Hughes et al. Vit D and respiratory health. Clinical and Experimental Immunology, 158: 20–25
Dosage of Vit.D

Vit.D supplementation – CORRECTION OF DEFICIENCY

- 10,000 IU daily or 60,000 IU weekly for 8-12 weeks
- 3,00,000 or 6,00,000 orally or by IM injections once or twice 3 months apart

Vit.D Maintenance

- 1000-2000 IU daily or 10,000 IU weekly or 60,000 IU once a month

THIS SHOULD BE ACCOMPANIED by CALCIUM INTAKE OF 1 GRAM/DAY
Conclusion

- Vitamin D receptors are found in most tissues, not just those participating in classic actions of vitamin D such as bone, gut, and kidney.

- These non classic tissues are therefore potential targets for active metabolite of vitamin D, 1,25(OH)$_2$D.

- Evidence suggests the usage and benefit in various indications like DM, Hypertension, Asthma, Influenza, Neurodegenerative diseases, etc.