Vitamin D Status in Children and Adolescents - An Indian Perspective

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Vitamin D Status in Children and Adolescents -
An Indian Perspective

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Introduction:

It is a well-known fact that Vitamin D is crucial for musculoskeletal health. Vitamin D is also required for contraction of muscles, nerve conduction and functioning of all cells of the body. Vitamin D deficiency has long been recognized as a cause of rickets in children and osteomalacia in adults. Prevention of vitamin D deficiency and achieving adequate vitamin D and calcium intake during childhood may reduce the risk of osteoporosis in later life.

Vitamin D is obtained from two sources, first by synthesis in the skin (amounts for which cannot be quantified) and in small amounts from the diet, hence determination of daily allowance of this vitamin is difficult. Further, the amount of vitamin D synthesized may differ with skin colour, season, pollution, etc., thus making the assessment even more difficult.

Just as there is no consensus on the amount of vitamin D recommended daily, similarly, there is no consensus on the concentrations of vitamin D below which children and adolescents are defined as vitamin D deficient or insufficient. Adults are classified as vitamin D deficient when 25-Hydroxyvitamin D [25(OH)D] concentrations are below 50 nmol/L and vitamin D insufficient if the concentration of 25(OH)D is between 50 to 80 nmol/L. Further, the concentrations of vitamin D must be interpreted in the context of the season, as higher concentrations are observed during summer months.

It is also well known that people living in countries at higher latitudes are more prone to seasonal vitamin D deficiency; this is possibly because wintertime sunlight does not promote conversion of the vitamin D precursor in the skin. However, in recent times, there are many reports from India and other sun-rich countries describing vitamin D deficiency in adults as well as children and adolescents. Lack of exposure to sunlight, outdoor activities under the sun, and physical activity coupled with poor vitamin D intake are believed to be the main associated factors for vitamin D deficiency in the young population.

In recent years, a wide variety of other conditions, such as autoimmune diseases, cardiovascular disease, cancers, type II diabetes and infectious diseases have also been shown to be associated with vitamin D deficiency.
Thus, the RDA of this important vitamin is not well defined, but a lot of deficiency and insufficiency has been reported in Indian children and adolescents. Further, vitamin D has also been linked with many non-musculoskeletal disorders. Hence, given the crucial nature of vitamin D, in this article we have briefly described the sources, structure, criteria for defining vitamin D deficiency and also reviewed reports on vitamin D deficiency in Indian children.

**Forms and sources of vitamin D:**

There are 2 forms of vitamin D viz. D₂ or ergocalciferol which is obtained from plant sources (ergosterol or provitamin D₂) and D₃ that is cholecalciferol which is synthesized in humans by the action of sunlight on the skin. As vitamin D can be synthesized in the skin, it is often called a prohormone, rather than a vitamin. The major source of Vitamin D is sunlight. Vitamin D₃ is synthesized in the skin by exposure to ultraviolet radiation in the band width of 290-315nm from 7-dehydrocholesterol. Exposure to sunlight for extended periods of time does not usually cause vitamin D toxicity. Within about 20 minutes of UVB exposure in light skinned individuals (a little longer for pigmented skin), the concentrations of vitamin D precursors produced in the skin reach an equilibrium and any further vitamin D that is produced in the skin is degraded.

Vitamin D can also be obtained in small amounts from the diet from oily fish such as trout, salmon, mackerel, herring, sardines, anchovies, pilchards, fresh tuna, cod liver and other fish liver oils, egg yolk and from
vegetarian sources such as mushrooms. It is also available from supplemented
breakfast cereals, hydro-genated fats (e.g. Dalda), formula milks and oil fortified
with Vitamin D. It is estimated that about one tenth of the body’s requirement is
derived from dietary sources in Indians.

**Criteria for deficiency:**

While there is no consensus on definitions of vitamin D deficiency and
sufficiency, serum 25(OH)D concentrations of <50 nmol/L are considered to
be lower than acceptable level by Lawson Wilkins Pediatric Endocrine
Society in the USA. The American Academy of Pediatrics in their revised
guidelines (2008), also state that on the basis of the available evidence, serum
25(OH)D concentrations in children should be > 50 nmol/L (20 ng/mL).

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<table>
<thead>
<tr>
<th>Vitamin D status</th>
<th>25(OH)D levels nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Deficiency</td>
<td>≤ 12.5</td>
</tr>
<tr>
<td>Deficiency</td>
<td>&lt; 37.5</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>&lt; 50</td>
</tr>
<tr>
<td>Sufficiency</td>
<td>50-250</td>
</tr>
</tbody>
</table>

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**Structure, Metabolism, Regulation and Functions:**

Vitamin D is a steroid-like substance which is fat soluble. After its synthesis in the
skin or absorption from the diet, it is carried by the bloodstream to the liver. In the
liver, it is converted into the 25-hydroxycholecalciferol (25(OH)D), calcidiol, which is
the major circulating and storage form of vitamin D and has some metabolic activity.
The 25(OH)D concentrations represent an individual's status of Vitamin D. However, 1,25(OH)_{2}D (calcitriol) is the most metabolically active form of vitamin D,
and is formed either in the kidneys or by the immune system. It induces the formation
of calcium transport involved in calcium absorption. It is believed that when
1,25(OH)_{2}D is synthesized by the monocyte-macrophage system, calcitriol acts
locally as a cytokine, defending the body against microbial invaders.

When synthesized in the kidneys, calcitriol circulates as a hormone and regulates
the concentrations of calcium and phosphate in the bloodstream. It promotes the
healthy mineralization as well as growth and remodeling of bone, and prevents hypocalcemic tetany. Blood calcium concentrations are maintained within narrow limits by the interplay of vitamin D and several hormones, including the parathyroid hormone (PTH), thyrocalcitonin, cortisol and steroids by controlling absorption, excretion and bone turnover. A lowering in calcium intake triggers an elevation in PTH concentrations and ultimately, an increase in calcium absorption and thus normalizes blood calcium. Enhanced degradation of 25(OH)D mainly, occurs in people who are suffering from chronic disorders like hepatitis and cirrhosis.\textsuperscript{17}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Regulation_of_Calcitriol_Synthesis.png}
\caption{Regulation of Calcitriol Synthesis}
\end{figure}

Many non-skeletal actions are also attributed to vitamin D\textsuperscript{18}. Organs such as the brain, prostate, breast, colon and immune cells have vitamin D receptors\textsuperscript{19}. Many studies indicate that levels of 25-hydroxyvitamin D below 50 nmol/L are associated with an increased risk of cancer\textsuperscript{20}. An association has also been reported between auto immune diseases and vitamin D\textsuperscript{21}. 

\begin{boxedquote}
Many studies indicate that levels of 25-hydroxyvitamin D below 50 nmol/L are associated with an increased risk of cancer. An association has also been reported between auto immune diseases and vitamin D
\end{boxedquote}
Measurement of vitamin D:

Measurements of 25(OH)D and 1,25(OH)₂D are largely used to assess the serum Vitamin D status. Serum concentrations of 25(OH)D are mainly used to assess an individual’s Vitamin D status as, the half life of 25(OH)D is approximately 3 weeks. In recent times 25(OH)D measurements are performed mainly by Radio Immuno Assay (RIA), High Pressure Liquid Chromatography (HPLC), Enzyme-Linked Immunosorbent assay (ELISA) or by Liquid chromatography Mass Spectroscopy (LCMS). 1,25 (OH)₂D is the physiologically active form of Vitamin D which is produced from 25OHD in the kidney (1 – α hydroxylase). Its half life is short (4-6 hours) and this metabolite can also be measured by Radio Immuno Assay, High Pressure Liquid Chromatography or Enzyme-linked immunosorbent assay.

![Diagram of Actions of Vit.D₃](image)

Fig. 3 Actions of Vitamin D

Requirements and Recommendations:

**India:** In spite of widespread vitamin D deficiency, as yet the National Institute of Nutrition, even in its current updated guidelines in 2010, does not give any specific recommendations for vitamin D intake as per different age groups. Their recent report states that vitamin D can be synthesized in the body in adequate amounts by simple exposure to bright sunlight even for 5 minutes per day. The report further
states that, increasing the RDI is not, but ensuring adequate exposure to sunlight is the solution to low vitamin D concentrations. The report recommends outdoor physical activity as the means of achieving adequate vitamin D status. However, under situations of minimal exposure to sunlight, a specific recommendation of a daily supplement of 400 IU (10 μg) is advised. The report does not specify the amount of time/ sunlight exposure which will ensure adequate vitamin D concentrations.

**American Academy of Pediatrics Revised Guidelines:** Since rickets attributable to low vitamin D (low intake, less sunshine exposure) continues to be reported from the United States and there are also concerns of deficiency in older children and adolescents, the American Academy of Pediatrics has in November 2008 published revised guidelines for Vitamin D intake. They recommend that all infants and children, including adolescents, have a minimum daily intake of 400 IU of vitamin D, starting soon after birth. Further, children who are at an increased risk of vitamin D deficiency (chronic fat malabsorption, children on chronic medication) may require higher doses of vitamin D. It is recommended that in these children, vitamin D status should be determined with laboratory tests and if vitamin D supplement is prescribed, 25-OH-D concentrations should be repeated at 3-month intervals until normal levels have been achieved.

The U. S. and Canadian governments asked the Institute of Medicine (IOM) to assess the current data on health outcomes associated with vitamin D and the IOM has suggested an intake of 400IU in infants up to 6 months and 600 IU thereafter. Recommended intakes from various European countries range from 200-400
Table 2: Recommendations for Vitamin D intake by various bodies

<table>
<thead>
<tr>
<th>NIN Hyderabad</th>
<th>American Academy of Pediatrics</th>
<th>National Academy of science/ Institute of Medicine</th>
<th>European countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under situations of minimal sun exposure 400IU/d</td>
<td>Infants and children- 400IU/D</td>
<td>For infants upto 1 year of age, 400IU/d</td>
<td>For 3 month old infants 400IU, 600 IU for 9 month olds</td>
</tr>
<tr>
<td>Adolescents- 400 IU/d</td>
<td>For 1-18 year old children and adolescents- 500IU/d</td>
<td>300 IU for 5 year olds and, 400 IU for 10 yrs olds</td>
<td>3001IU for 15 yr olds (data are means)</td>
</tr>
<tr>
<td>Higher doses and monitoring of Vit D for children at increased risk of vitamin D deficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Causes of vitamin D Deficiency in a Sun-rich Country:
There is evidence that low dietary calcium intake may play a major role in the pathogenesis of nutritional rickets in sun rich countries such as India. Ethnicity/genes may also be an important reason for vitamin D deficiency in India. More recently, it has also been shown that an increment in serum 25(OH)D in response to treatment depends on the heritability of vitamin D binding protein. Other factors that are known to affect vitamin D concentrations are season, body mass index, reduced physical activity, increased pollution and darker skin colour.

Table 3. Causes of Vitamin D Deficiency

| Decreased vitamin D synthesis |
| Skin pigmentation |
| Physical agents blocking UVR exposure |
| Sunscreen, clothing |
| Shade |

| Geography |
| Latitude, season |
| Air pollution, cloud cover, altitude |

| Decreased nutritional intake of vitamin D |
| Decreased maternal vitamin D stores and exclusive breastfeeding |
| Malabsorption (celiac disease, pancreatic insufficiency, cystic fibrosis, biliary obstruction, biliary atresia) |
| Decreased synthesis or increased degradation of 25(OH)-D (chronic liver disease and drugs such as rifampicin, isoniazid, anticonvulsants) |
Vitamin D Deficiency: Reports from India

Vitamin D is crucial at every stage of the life cycle. In recent years there have been many reports of vitamin D deficiency in Indian children and adults. However, there are also reports of vitamin D deficiency rickets in preschool children from the seventies\textsuperscript{17}. The renewed interest in vitamin D is perhaps due to its effect not only on the musculoskeletal system, but also its role in the reduction of other systemic diseases such as type I diabetes, cancers and infectious diseases\textsuperscript{18}. Table 4 summarizes reports of vitamin D deficiency from India.

Pregnant mothers: In a study from Lucknow, 84% women (84.3% of urban and 83.6% of rural women) had 25(OH)D values below the cutoff, while the mean cord blood 25(OH)D value of the total cohort was only 21 nmol/L\textsuperscript{28}. In another study on pregnant women in the second trimester, seventy-four percent of rural pregnant women had vitamin D deficiency. Mean 25OHD of these women in summer was 27.3 nmol/L\textsuperscript{29}. Studies have also highlighted associations between maternal nutritional status during pregnancy and bone mass in the offspring\textsuperscript{30}. In a study to examine the association between maternal vitamin D status, anthropometric variables, body composition, and cardiovascular risk markers in Indian children, authors found that 67% women had 25OHD concentrations below 50nmol/L at the time they delivered. At ages 5 and 9.5 y, children born to vitamin D–deficient mothers had smaller arm-muscle area in comparison with children born to mothers without deficiency\textsuperscript{31}.

Thus, several studies report low vitamin D concentrations during pregnancy, both from rural and urban areas and there is urgent need for public health intervention. Vitamin D stores of the newborn depend entirely on the vitamin D stores of the mother. The newborn infant born to a vitamin D replete mother is protected from vitamin D deficiency for the first few months of life as 25(OH)D crosses the placenta readily and neonatal levels

If the mother is vitamin D-deficient, the infant will be deficient because of decreased maternal foetal transfer of vitamin D.
approximate two thirds of maternal serum concentrations\textsuperscript{32}. Hence, if the mother is vitamin D-deficient, the infant will be deficient because of decreased maternal foetal transfer of vitamin D\textsuperscript{33}.

**Exclusively breast fed infants:** Milk from the mother whose diet is sufficient and properly balanced will supply all the necessary nutrients except fluoride and vitamin D\textsuperscript{34}. In a study on exclusively breast fed infants and their mothers, authors have reported 25(OH)D concentrations of 42 nmol/L in exclusively breast fed infants. In their study population, as a whole, 54 (55.87\%) and 43 (44.33\%) out of 97 infants had mean serum 25(OH)D levels <27.5 nmol /L at 10 weeks and 6 months, respectively\textsuperscript{35}. In another study on 2-24 week old breast fed infants, low serum 25(OH)D levels <25 nmol/l (10 ng/ml) were found in 43.2\% of the infants\textsuperscript{36}. In a study to determine the prevalence of vitamin D deficiency and insufficiency [serum 25 hydroxyvitamin D 25(OH)D < 37.5 nmol/L and 37.5-50 nmol/L, respectively] among healthy term breast-fed 3 month old infants, authors found that Vitamin D deficiency was present in 66.7\% of infants and insufficiency in an additional 19.8\% of infants. Authors also found Radiological Rickets was found in 30.3\% of infants with 25(OH)D < 25 nmol/L. sunlight exposure and mother’s 25(OH)D were predictors of infants’ 25(OH)D levels\textsuperscript{37}. Thus, many studies report a high prevalence of vitamin D deficiency in healthy infants highlighting the need to develop recommendations for vitamin D supplementation for young infants.

**Toddlers and preschool children:** The peak age at which rickets is most prevalent is 3-18 months of age and factors which are important in the pathogenesis of rickets at this age include continued exclusive breast-feeding, living in temperate climates, lack of sunlight exposure and dark pigmented skin. In a hospital based study from Delhi, toddlers with a mean age of 1.6 years who were brought to a tertiary level care
centre with a history delayed walking were studied. Sixty percent of these children were diagnosed to have nutritional rickets. In a study to determine whether subclinical vitamin D deficiency in Indian children under 5 y of age is a risk factor for severe acute lower respiratory infection, authors found that children with severe respiratory tract infection had vitamin D levels of 22.8 nmol/L, which were much lower than that of controls. In a study looking at the 25 (OH) D levels in slum children from three areas in Delhi, authors found evidence of widespread vitamin D deficiency.

Subclinical vitamin D deficiency in Indian children under 5 y of age is a risk factor for severe acute lower respiratory infection, children with severe respiratory tract infection had vitamin D levels of 22.8 nmol/L, which were much lower than that of controls.

While in one group of children from slums there were 2% children below the cut-off (35nmol/L), in the other two slums percentage prevalence of vitamin D deficiency was over 80%40. A study from Pune describes the role of sunlight exposure in determining the vitamin D status of underprivileged toddlers. Underprivileged toddlers who were deprived of sunlight had a much greater incidence of hypovitaminosis D (77%) and frank rickets than control group (16.4%)41. In a study to compare the vitamin D status of 34 children, 9–24 months old, living in an area of Delhi renowned for high levels of atmospheric pollution (Mori Gate), with a comparable age matched group of children from a less polluted (Gurgaon) area of the city, authors found that children living in areas of high atmospheric pollution were at risk of developing vitamin D deficiency rickets42.

These studies underscore the fact that vitamin D deficiency is still common in Indian toddlers.

Adolescents: In a study reporting Vitamin D concentrations in girls from two socio economic classes from Delhi, mean serum vitamin D was found to be 32 nmol/L43. A study

Underprivileged toddlers who were deprived of sunlight had a much greater incidence of hypovitaminosis D (77%) and frank rickets.
from Lucknow also reports low vitamin D concentrations in 10-18 year old healthy children and adolescents. Results have been reported by other studies from India. Our own studies in underprivileged girls from Pune have also shown that there is a high prevalence of hypovitaminosis D."
Table 4. Studies from different parts of India depicting a high incidence of vitamin D deficiency in the population

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Publication</th>
<th>Place</th>
<th>Population</th>
<th>Age</th>
<th>Vitamin D</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>AJCN 2011</td>
<td>Mysore</td>
<td>Women delivering at hospital in Mysore</td>
<td>24 years</td>
<td>39.3 nmol/L</td>
<td>Intrauterine exposure to low 25 (OH)D is associated with less muscle mass and higher insulin concentrations is associated with less muscle mass and higher insulin resistance in\textsuperscript{31}</td>
</tr>
<tr>
<td>2.</td>
<td>IJMR 2011</td>
<td>Delhi</td>
<td>Full term infants</td>
<td>2.5 to 3.5 months</td>
<td>10.1 ng/ml</td>
<td>Prevalence of vitamin D deficiency and insufficiency was found to be high in breastfed infants and their mothers, with radiological rickets in a third of infants with 25(OH)D&lt;10 ng/ml in this study\textsuperscript{37}</td>
</tr>
<tr>
<td>3.</td>
<td>Indian Pediatrics 2011</td>
<td>Delhi</td>
<td>LSE and HSE</td>
<td>6 - 17 years</td>
<td>LSE-31.2-32.9 nmol/l, HSE-29.1-30.8 nmol/l</td>
<td>At baseline, 93.7% school-girls were vitamin D deficient [25 (OH)D&lt;50 nmol/L], 60,000 IU of cholecalciferol, monthly or two-monthly, resulted in a significant increase in serum 25(OH)D levels in vitamin D deficient school-girls.\textsuperscript{45}</td>
</tr>
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Table 4. Studies from different parts of India depicting a high incidence of vitamin D deficiency in the population

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<tbody>
<tr>
<td>4.</td>
<td>ACTA Pediatrica 2010</td>
<td>Delhi</td>
<td>Infants at 6 months</td>
<td>6 months</td>
<td>16.9 ng/ml</td>
<td>Exclusively breastfed infants and their mothers are Vitamin D deficient, hence the need to improve vitamin D status(^\text{35})</td>
</tr>
<tr>
<td>5.</td>
<td>Clinical Endocrinology 2009</td>
<td>Barabanki district - near Lucknow</td>
<td>Rural girls and pregnant women</td>
<td>14.3, 26.7 years</td>
<td>33.3, 37.8 nmol/L</td>
<td>Authors report a high prevalence of vitamin D deficiency among pregnant women and adolescent girls from a rural Indian setting(^\text{39})</td>
</tr>
<tr>
<td>6.</td>
<td>Indian Pediatrics 2009</td>
<td>Delhi</td>
<td>Exclusively breast-fed infants</td>
<td>2 - 24 weeks</td>
<td>28.9 nmol/L</td>
<td>A high prevalence of vitamin D deficiency was found in lactating mothers and their exclusively breast fed infants. Infants born to mothers with hypovitaminosis D had 3.8 times higher risk of developing hypovitaminosis D as compared to those born to mothers with normal vitamin D levels(^\text{36})</td>
</tr>
</tbody>
</table>
Table 4. Studies from different parts of India depicting a high incidence of vitamin D deficiency in the population

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<tr>
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<th>Conclusions</th>
</tr>
</thead>
</table>
| 7.     | IJP 2001               | Pune                | Slum dwelling toddlers    | 2.6 years | 113, 9.6 nmol/L | Underprivileged toddlers who were deprived of sunlight had a much greater incidence of hypovita-minosis D and frank rickets. The study has important public health implications and underscores the necessity for sun-light exposure in young children.\
                                                                 |                                                     |                                                       |                                                     | 41 |
| 8.     | IJMR 2008              | Andhra Pradesh      | Rural and Urban boys and girls | Rural (11-13.6 years) Urban (11.6 - 13.3 years) | Rural male - 17 Rural female - 19 Urban male - 15.6 Urban female - 18.5 ng/ml | The 25(OH)D levels of both the urban and rural children were low. Low 25(OH)D levels were associated with a deleterious effect on bone mineral homeostasis.\
<pre><code>                                                             |                                                     |                                                       |                                                     | 46 |
</code></pre>
<p>| 9.     | Archives of disease in childhood | Pune                | LSE girls                | 14.7 years | 24 nmol/L       | 70% girls had hypovita-minosis D and dietary calcium intake should be considered when assessing the adequacy of an individual’s vitamin D status. |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>10.</td>
<td>AJCN 2005</td>
<td>Lucknow</td>
<td>Pregnant women and new borns</td>
<td>24.4 years</td>
<td>14.9 ng/ml, cord blood 8.3 ng/ml</td>
<td>A high prevalence of physiologically significant hypovitaminosis D among pregnant women and their newborns was found, the magnitude of which warrants public health intervention.</td>
</tr>
<tr>
<td>11.</td>
<td>Indian Pediatrics 2010</td>
<td>Delhi</td>
<td>Apparently healthy children from 2 SE classes</td>
<td>11.7 years</td>
<td>30 nmol/L</td>
<td>A high prevalence of hypovitaminosis D exists in apparently healthy children in Delhi.</td>
</tr>
<tr>
<td>12.</td>
<td>EJCN 2004</td>
<td>Indapur</td>
<td>80 cases with severe lower resp. tract infections and 70 controls</td>
<td>22.8 (cases), 38.4 (controls) nmol/L</td>
<td>Subclinical vitamin D deficiency and non-exclusive breast feeding in the first 4 months of life were significant risk factors for severe ALRI in Indian children.</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Indian Pediatrics 2004</td>
<td>Delhi</td>
<td>100 infants and children with rickets from slum</td>
<td>9-30 months</td>
<td>20.2 nmol/L and 96.3 nmol/L</td>
<td>Vitamin D deficiency is widespread in some parts of Delhi. The findings of the study make authors suspect that other facts may be involved and the poor vitamin D levels may not be explained fully on the basis of pollution and poor UV light.</td>
</tr>
</tbody>
</table>
Table 4. Studies from different parts of India depicting a high incidence of vitamin D deficiency in the population

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</table>
| 14.    | IJMR 2008        | Delhi   | 555 healthy School children              |             |                            | Children from LSES had significantly lower BMD at forearm compared to those from USES
d                                           |
| 15.    | J. Trop Ped. 2003 | Lucknow | Children and adolescents with rickets/ osteomalacia and controls | 2.5 & 14.8 years | 55.5 (toddlers) 12.6 (adolescents with osteomalacia, 46 nmol/L (control adolescents) | Deficient calcium intake is universal among children and adolescents with rickets/ osteomalacia. Inadequate sun exposure and vitamin D deficiency are important in the etiology of adolescent osteomalacia. |
Hypervitaminosis D:

An overdose of Vitamin D causes hypercalcemia, which may result in anorexia, nausea, and vomiting, polyuria, polydipsia, weakness, nervousness, pruritus, and renal failure. Proteinuria, urinary casts, azotemia, and metastatic calcification (especially in the kidneys) may develop. In healthy adults, intake of more than 50,000 IU/day may cause toxicity over several months. Maternal hypercalcemia during pregnancy may increase fetal sensitivity to vitamin D and can lead to a syndrome of mental retardation and facial deformities\(^{11}\). Pregnant or breastfeeding women should thus be prescribed vitamin D supplements with care. The Institute of Medicine has recently increased the tolerable upper limit (UL) to 2500 IU per day for ages 1–3 years, 3000 IU per day for ages 4–8 years and 4000 IU per day for ages 9–71+ years (including pregnant or lactating women)\(^{23}\). Vitamin D toxicity is treated by discontinuing vitamin D supplementation and restricting calcium intake. Treatment of vitamin D intoxication focuses on control of hypercalcemia. Rehydration using normal saline, often in conjunction with a loop diuretic to increase calcium excretion is used. Glucocorticoids decrease intestinal absorption of calcium and prednisone in a dose of 1–2 mg/kg/24 hr may be used\(^{48}\).

Treatment of deficiency states:

High dose vitamin D therapy is believed to be an effective method for treating established or recalcitrant vitamin D deficiency. It involves oral or intramuscular administration of the total treatment dose of vitamin D 600 000 IU either as a single dose or as oral vitamin D3 at a dose of 2000-6000 IU producing radiologic clearing, for 4-6 weeks. Vitamin D deficiency resulting due to conditions other than nutritional states require larger doses or different preparations. Table 5 summarizes the doses of vitamin D prescribed in deficiency states by various authors.
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Indication</th>
<th>Dose</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Vitamin D deficiency</td>
<td>Start on 25(OH)D2 2000–4000 IU x 4-6 weeks Or 6000 IU/day x 10 days Or 6000 IU/day weekly for 10 weeks Or 20000 IU/day for 1 month Or 800 IU/day x 3-4 months Or 3 lac IU im &lt;1 yr, 6 lac in &gt;1 yr (Stoss therapy)</td>
<td>AAP recommendation(^{15}), Nelson's text book(^{68})</td>
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<td>2.</td>
<td>Hypoparathyroidism</td>
<td>0.03 µg/kg/day D3 (0.5-1 µg/day) for 3-4 days Shift to: Vit D2 50 µg/kg/day 3-4 weeks</td>
<td>Rude RK(^{69})</td>
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<td>3.</td>
<td>Familial Hypophosphatemic Rickets</td>
<td>Vit D3 – 20-30 ng/kg/day (1-2 µg/day)</td>
<td>Russell W.(^{50})</td>
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<td>4.</td>
<td>Uremia</td>
<td>Vit D3 – 10-20 ng/kg/day Or Vit D2 &lt;5 ng/ml – 8000 IU/day x 4 wk 400 IU/day x 8 wk 5-15 ng/ml - 4000 IU x 12 wk 15-30 ng/ml - 2000 IU x 12 wk</td>
<td>Wesseling K.(^{51})</td>
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<td>5.</td>
<td>Osteoporosis</td>
<td>Vit. D2 – 600000 x 10 days Vit. D 400-1000 IU/day maintenance</td>
<td>Maalouf NM et al(^{52})</td>
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</tbody>
</table>
Prevention:
Vitamin D supplementation to all infants should begin during the first days of life as there is a high risk of sub clinical vitamin D deficiency, even in regions with a temperate climate. The American Academy of Pediatrics also recommends that children and adolescents who do not get regular sunlight exposure and do not ingest at least 500 ml/day of vitamin D fortified milk also require 400IU of vitamin D/day\textsuperscript{15}.

Conclusions:
Vitamin D plays a key role in bone health and is also important in non-skeletal disorders including autoimmune disorders, infections and cancers. It has become increasingly evident that abundant sunshine does not seem to protect Indians from widespread vitamin D deficiency. Urgent public health measures are thus warranted to prevent vitamin D deficiency in Indian children and adolescents.

References:


