Abstract
Vitamin D deficiency is endemic to South Asia, and is associated with varied biochemical and clinical presentations. Health care professionals of all specialties need to ensure optimal Vitamin D level of all persons, irrespective of age or gender, to prevent the many complications that are associated with vitamin D deficiency. These pragmatic recommendations aim to support health care professionals in assessing, preventing and treating vitamin D deficiency, in a rational manner.

Keywords: Osteomalacia, Rickets, Vitamin D.

Physiology
Vitamin D, also known as cholecalciferol, the sunshine vitamin, or anti-rachitic vitamin, is actually a hormone. Cholecalciferol is synthesized in the skin by exposure to ultraviolet light, and then hydroxylated at 25 and 1 carbon positions, in the liver and kidneys, to produce 25-hydroxy vitamin D, (25(OH)D) and 1,25 dihydroxy vitamin D (1,25(OH)2D) respectively. Small amounts of vitamin D may be derived from dietary sources such as fish oil.

Vitamin D acts on vitamin D receptors (VDR) in target cells, where it forms heterodimers with the retinoid X receptor (RXR), which activate vitamin D target genes. Vitamin D’s main function is to regulate calcium and phosphate metabolism, in the intestine, bone and kidneys. In coordination with parathyroid hormone and fibroblast growth factor 23, Vitamin D increases calcium absorption from the intestine, enhances calcium reabsorption from the kidney, and promotes bone formation. Apart from its skeletal effects, vitamin D is also thought to fulfill many extra skeletal roles. These include facilitation of insulin secretion, innate immunity, cardiovascular health and anti-neoplastic defense. Research is ongoing in these fields.

Normal Values
Vitamin D (25(OH) D) levels between 20 and 40ng/ml (50 and 100 nmol/l) are considered optimal for the majority of people. These levels are associated with minimal adverse clinical effects such as fractures and falls. Vitamin D levels of above 30ng/ml are optimal for patients with osteoporosis, or older adults (>50 years) at high risk of osteoporosis.

Vitamin D in South Asia
As sunlight and the skin are the main sources of vitamin D, alterations in sunlight exposure of skin may modify vitamin D levels. Darker skinned individuals, and those whose skin is not exposed to sunlight because of clothing, sunscreen use, or lack of outdoor activities, may have lower vitamin D levels. Ultraviolet irradiation is reduced during winter, in temperate latitudes (as opposed to tropical or equatorial latitudes), and by the presence of air pollution. All these factors contribute to vitamin D deficiency.

Numerous studies on high prevalence of hypovitaminosis D in both rural and urban areas in adults, the elderly, antenatal women, children, infants and neonates have shown that vitamin D levels of neonates correlate with their mothers. The common clinical presentations of vitamin D deficiency are listed in Table-1.

It is difficult to achieve currently recommended vitamin D levels with sunlight exposure alone. Sunlight exposure of 15-30% of total body surface area, for 30 minutes, between 11 am and 3 pm, during summer, (when the sun is at its zenith) is able to achieve an increase of 4 ng/ml in children.

Table-1: Clinical presentation of vitamin D deficiency.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Infants</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficult breathing, irritability</td>
<td>Repeated infection, bone pains, difficulty in squatting/standing/walking</td>
<td>Bone pains, muscle pain, muscle weakness, difficulty in squatting/standing/walking</td>
<td>Wadding gait, anterior tibial weakness, Rib cage tenderness, fractures</td>
</tr>
<tr>
<td>Seizures, Tetany</td>
<td>Hypotonia, delayed dentition, enamel hypoplasia, dental caries, wrist widening</td>
<td>Rachitic rosary, Knock knees, Bow legs.</td>
<td>Pelvic deformities, Kyphoscoliosis</td>
</tr>
<tr>
<td>Stridor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated cardiomyopathy, Craniotubes, open anterior fontanelle, frontoparietal bossing</td>
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</tbody>
</table>
Vitamin D Screening
Universal screening for vitamin D levels is not recommended. However, screening with 25 (OH) vitamin D should be considered in persons with
- Symptoms/signs suggestive of
  - osteomalacia
  - osteoporosis
  - musculoskeletal disease
  - high risk factor for vitamin D deficiency
  - inflammatory bowel disease
  - bariatric surgery
  - chronic kidney disease
  - drug use
- antiepileptic
- antitubercular
- glucocorticoids
- antiretroviral
- ketoconazole

Extra indications of measurement of 25 (OH) D in children include
Late onset hypocalcaemic seizures
Dilated cardiomyopathy
Rickets
Cancer
Organ transplant recipients
Chronic inflammatory rheumatic disease
Juvenile idiopathic arthritis
Ankylosing spondylitis

1, 25 (OH) 2 D testing is indicated in:
- chronic kidney disease
- phosphate-losing bone disease
- oncogenic osteomalacia
- Vitamin D- resistant rickets
- Chronic granulomatous disease
- Sarcoidosis
- Lymphoma

Supplementation
The recommended vitamin D intake for South Asians is 600-1000 IU/day for healthy adults aged less than 50 years, and 800-2000 IU/day for high risk individuals and older adults. The upper range of these doses should be preferred in South Asians. Doses of up to 4000 IU/day do not require monitoring, while doses of 10000 IU/day are not associated with toxicity.

Treatment
Vitamin D deficiency is treated or prevented with cholecalciferol, which is available in drop, capsule, sachet, suspension, and injectable form. Cholecalciferol is also

Table-2: Treatment options with cholecalciferol in adults.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Description</th>
<th>Indications/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly</td>
<td>60000 IU weekly x 8 weeks, followed by 60000 IU/month life</td>
<td>Asymptomatic persons with very low vitamin D (&lt; 10 ng/ml)</td>
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<tr>
<td></td>
<td></td>
<td>Metabolic bone disease (rickets, osteomalacia)</td>
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<tr>
<td></td>
<td></td>
<td>Double dose may be used in obesity, malabsorption, concomitant anti-tubercular and anticonvulsant therapy</td>
</tr>
<tr>
<td>Monthly</td>
<td>60000-120000 IU per month, life long</td>
<td>Apparently healthy subjects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60000 IU in summer and 120000 IU in winter</td>
</tr>
<tr>
<td>Daily</td>
<td>1000-2000IU/day, with or without calcium, life long</td>
<td>Mild vitamin D deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elderly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregnancy / lactation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prevention</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance therapy</td>
</tr>
<tr>
<td>Parenteral mega dose</td>
<td>300000-600000 IU per 6 months</td>
<td>Limited oral absorption</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor compliance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not recommended as first line (significant variation in absorption: risk of hypercalcemia)</td>
</tr>
</tbody>
</table>

Table-3: Treatment options with cholecalciferol in special situations.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Description</th>
<th>Indications/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASYMPTOMATIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants</td>
<td>400 IU/day</td>
<td>Begin within first few days of birth: continue through infancy</td>
</tr>
<tr>
<td>Children</td>
<td>600-1000 IU/day or 60000 IU once in 2-3 months</td>
<td>Continue through childhood</td>
</tr>
<tr>
<td>Adolescents</td>
<td>1000IU/day in all; 2000 IU/day in obese</td>
<td>Continue through adolescence</td>
</tr>
<tr>
<td>SYMPTOMATIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants</td>
<td>1000-2000 IU/day x 8-12 weeks</td>
<td>No role for weekly regimen</td>
</tr>
<tr>
<td>Children</td>
<td>2000-4000 IU/day x8-12 weeks</td>
<td>Alternative 60000 IU every 14 days: x 8-12 weeks</td>
</tr>
<tr>
<td>Adolescents</td>
<td>4000-6000 IU/day x 8-12 weeks</td>
<td>15000 IU stat; repeat after 6 weeks if necessary</td>
</tr>
<tr>
<td>Pregnancy 2nd and 3rd trimesters; lactation</td>
<td>1000 IU/day for all; 2000 IU/day in high risk/deficient women</td>
<td>Alternative 300000 IU stat; repeat after 6 weeks if necessary</td>
</tr>
<tr>
<td>Chronic kidney disease/renal transplant: Documented vitamin D deficiency</td>
<td>60000 IU weekly x 8 weeks, followed by 60000 IU/month life</td>
<td>Weekly or monthly doses are not recommended</td>
</tr>
<tr>
<td>Chronic kidney disease-deficiency not documented; non-deficient renal transplant recipients; chronic liver disease</td>
<td>Maintenance: 60000 IU/ month or 2000 IU daily</td>
<td>Monitor serum calcium every 3 months in renal disease; at least once in liver disease</td>
</tr>
</tbody>
</table>
Vitamin D deficiency: Pragmatic suggestions for prevention and treatment

included in many fixed dose combinations of calcium and vitamins. Various studies have shown the benefits of supplementing Vitamin D in Indian populations.\textsuperscript{19-26}

Four options are available for use in adults (Table-2). Table-3 lists regimes and doses for infants, children, adolescents, antenatal women, and special populations such as chronic kidney disease and chronic liver disease. Adequate calcium intake must be ensured (30-75 mg/kg/day in children).

**Summary**
This communication describes the etiopathogenesis, symptoms and signs of Vitamin D deficiency. Through the pragmatic suggestions listed herein, we aim to support health care professionals in assessing, preventing and treating Vitamin D deficiency, in a rational manner.

**References**


