Prevention of Rickets and Vitamin D Deficiency

MAT-IN-2200454 v1.0 02/22

Learning Objectives

- To provide an overview on the prevalence of vitamin D deficiency among children
- To get an insight into an overview of rickets in children
- To review the supporting clinical evidences on the efficacy of vitamin D supplementation
- To discuss the clinical use of vitamin D supplementation with respect to a case scenario

Section 1:

Prevalence of Vitamin D Deficiency Among Children

Prevalence of Hypovitaminosis D and Development of Rickets in Indian Toddlers

Anthropometric and biochemical characteristics of study subjects

Parameters	Group A (Outdoor Children)		Group B (Indoor Children)	
	Male (n=25)	Female (n=25)	Male (n=31)	Female (n=29)
Age (yr)	2.26±0.8	2.53±0.8	2.94±0.6**	2.70±0.6^{ns}
Height z score	–2.2±1.6	–1.9±1.1	–1.5±1.2**	–1.6±1.4^{ns}
Weight z score	–1.2±1.5	–1.7±0.8	–1.4±0.73*	–1.4±1.0^{ns}
Hemoglobin (mmol/L)	6.14±1.1	6.6±0.8	6.4±0.1^{ns}	6.0±1.0*
ALP U/L	492±105	570±138	1039±460**	1094±445**
25OHD[a] (nmol/L)	95.86 (91.6)	130.2 (67.7)	14.0 (32.0)**	5.2 (21.1)**
PTH[a] (pmol/L)	46.0 (44.0)	62.0 (80.2)	91.2 (84.3)**	95.6 (119.9)^{ns}
Serum phosphorus (mmol/L)	1.8±0.2	2.0±0.2	1.7±0.2*	1.7±0.3*
Serum ionic calcium (mmol/L)	1.0±0.02	1.0±0.05	0.9±0.17*	0.9±0.2*
Energy (kcal)	905±422	766±383	1513±464**	1382±458**
Protein (g)	26.8±16.3	22.2±17.9	35.2±11.2**	31.3±11.1**
Calcium (mg)	216±222	288±196	292±124^{ns}	251±101^{ns}
Phosphorus (mg)	581±364	523±357	620±219^{ns}	555±203^{ns}

[a]Values are median and inter-quartile range.
*p<0.05, **p<0.01, ns-not statistically significant.

Prevalence of hypovitaminosis D was **77%** in group B toddlers (46 of 60) and **16.4%** (10 of 61) had rickets, while none of the group A toddlers had 25OHD levels below 30 nmol/L.

Ekbote VH, *et al. Indian J Pediatr*. 2010;77:61–5.

ALP: Alkaline phosphatase activity; PTH: Serum parathyroid hormone; 25OHD: 25 Hydroxy vitamin D

High Prevalence of Vitamin D Deficiency in Breastfed Infants

Prevalence of vitamin D deficiency and its biochemical markers in infants and mothers (n=98)

Parameter	Infants n (%)	Mothers n (%)
Vitamin D deficiency	64 (66.7)	77 (81.1)
Vitamin D insufficiency	19 (19.8)	11 (11.6)
Severe vitamin D deficiency	26 (27.1)	22 (23.2)
Hypocalcemia	7 (7.1)	23 (24.2)
Raised ALP	89 (91.8)	92 (96.8)
Hyperparathyroidism	47 (48.5)	52 (53.7)

Vitamin D deficiency was found in 66.7% of infants and 81.1% of mothers.

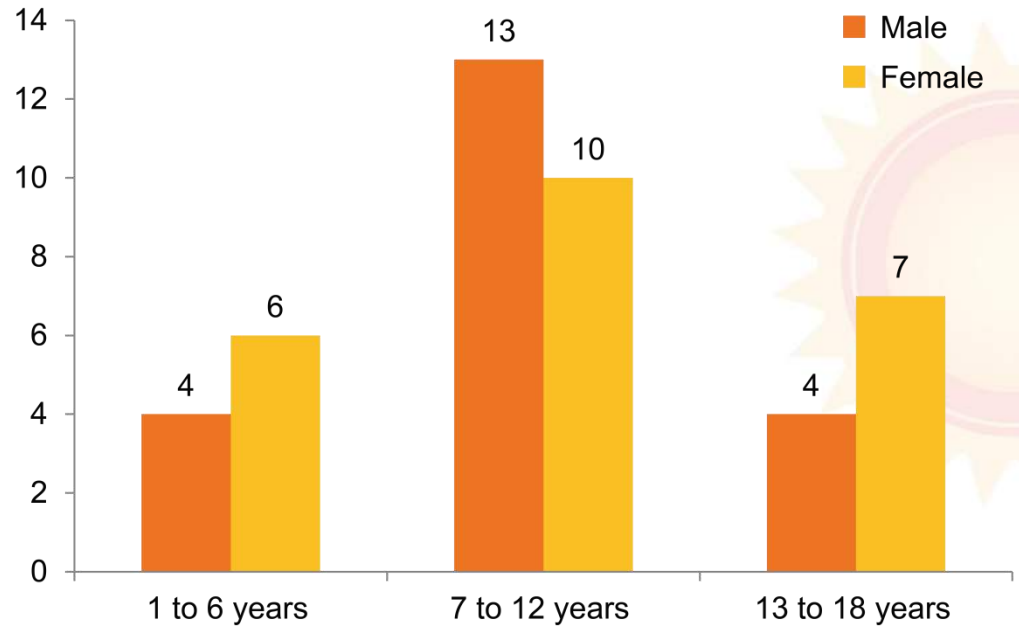
Radiological rickets was present in 30.3% of infants with 25OHD <10 ng/mL.

ALP: Alkaline phosphatase activity; 25OHD: 25 Hydroxy vitamin D

Jain V, et al. Indian J Med Res. 2011;133:267–273.

Prevalence of Skeletal Deformity due to Nutritional Rickets in Children Between 1 and 18 Years

Age-wise distribution of skeletal deformities due to nutritional rickets



- Of the 16,274 tea garden children included in this study (male and female) of the age-group 1–18 years, 44 had skeletal deformity due to nutritional rickets.
- The majority of children with deformities (57.27%) were between 7 and 12 years.

Chabra T, *et al. J Clin Orthop Trauma*. 2016;7:86–89.

Section 2:

An Overview of Rickets in Children

Pathogenesis and Types of Rickets

Types of rickets

Calcipenic rickets

- **Vitamin D deficiency or resistance**
  - Dietary deficiency
  - Malabsorption
  - Lack of sunlight exposure
  - Defect in 25 hydroxylation of vitamin D (e.g., liver disease, medications such as phenytoin)
  - Failure of 1 hydroxylation of vitamin D due to inherent deficiency of 1 alpha hydroxylase secondary to defects in the 1 alpha hydroxylase gene (VDDR I)
  - End-organ resistance to vitamin D (VDDR II)
- **Calcium deficiency**
- **Renal rickets secondary to CKD**

Phosphopenic rickets

Renal tubular phosphate loss

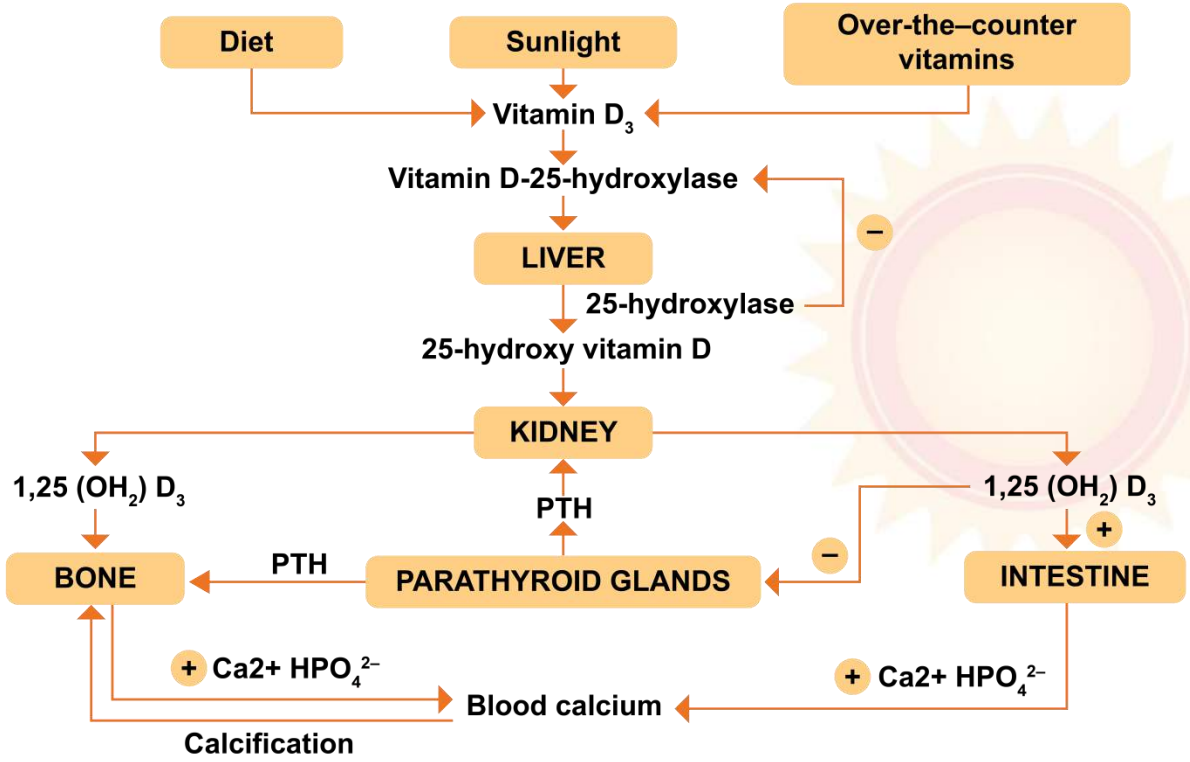
- Isolated phosphate loss secondary to genetic mutations:
  - XLHR
  - ARHR
  - ADHR
  - Hypophosphatemic rickets with hypercalciuria
- Renal Fanconi syndrome
- Dietary phosphate deficiency
- Phosphate malabsorption

ADHR: Autosomal dominant hypophosphatemic rickets; ARHR: Autosomal recessive hypophosphatemic rickets; CKD: Chronic kidney disease; VDDR: Vitamin D–dependent type 1 rickets; XLHR: X-linked hypophosphatemic rickets.

Chanchlani R, *et al. Kidney Int Rep.* 2020 Apr 11;5(7):980-990.

Calcipenic Rickets: Sources and Metabolism of Vitamin D

Sources and metabolism of vitamin D



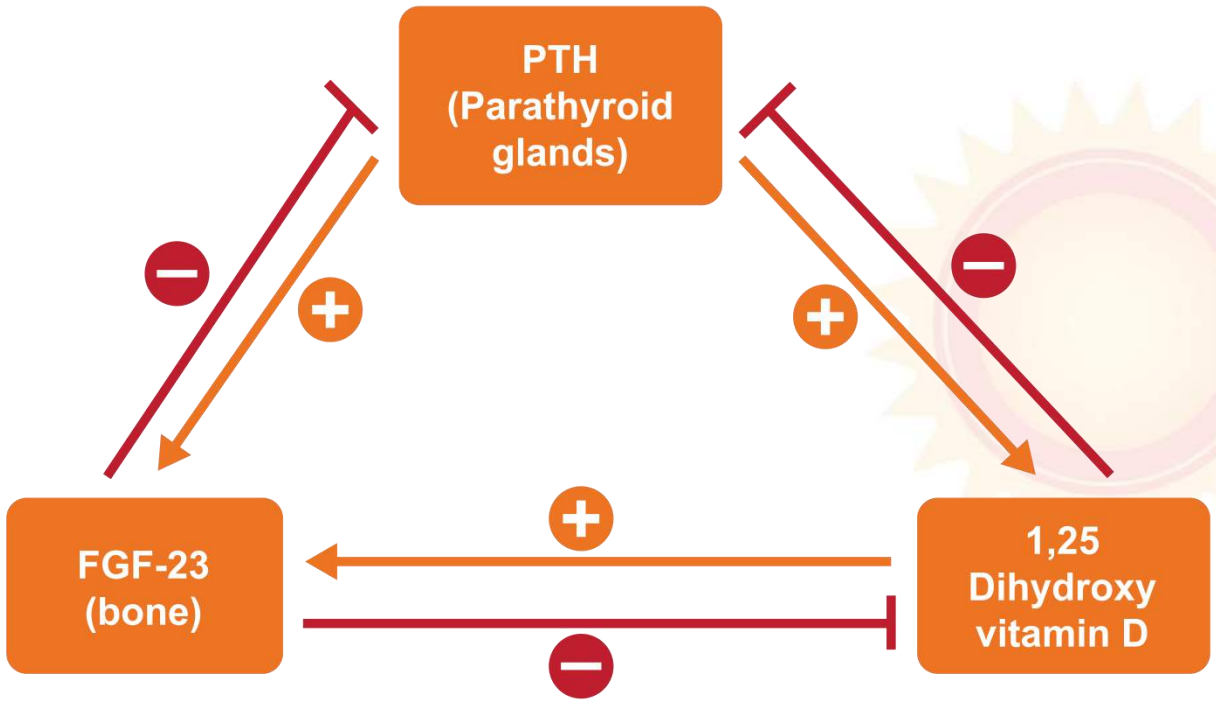
- Calcipenic rickets, as the name suggests, happens primarily because of a lack of calcium, which is most commonly due to a low availability or defective functioning of vitamin D in the body.
- Vitamin D plays an essential role in skeletal health by regulating normal blood levels of calcium and phosphorus as presented on the slide.

PTH: Parathyroid hormone

Chanchlani R, *et al. Kidney Int Rep.* 2020 Apr 11;5(7):980-990.

Calcipenic Rickets: Parathyroid/Bone/Kidney Axis

Parathyroid/bone/kidney axis



1. PTH increases 1,25 dihydroxy vitamin (vit) D synthesis in the kidney.

2. FGF-23 is produced by bone and it acts on the kidney.

3. FGF-23 decreases PTH and 1,25 dihydroxy vitamin D.

4. Both PTH and 1,25 dihydroxy vitamin D increase FGF-23 synthesis.

FGF-23 : Fibroblast growth factor 23 ; PTH: Parathyroid hormone

Chanchlani R, *et al. Kidney Int Rep.* 2020 Apr 11;5(7):980-990.

Nutritional Rickets/Vitamin D Deficiency Rickets

Severity of 25 (OH) vitamin D deficiency

Vitamin D status	ng/mL
Deficiency	<30
Insufficiency	30–50
Adequate	>50
Toxicity	>250

Nutritional rickets is the most common form of bone disease, primarily affecting infants and young children.

Vitamin D regulates calcium and phosphorus in the blood, and deficiency of vitamin D does result in inadequate mineralization of osteoid produced by osteoblasts.

The primary cause of vitamin D deficiency usually involves interplay of nutritional inadequacy and lack of sunlight exposure with overlapping contributions by cultural, environmental, and genetic factors.

Chanchlani R, *et al. Kidney Int Rep.* 2020 Apr 11;5(7):980-990.

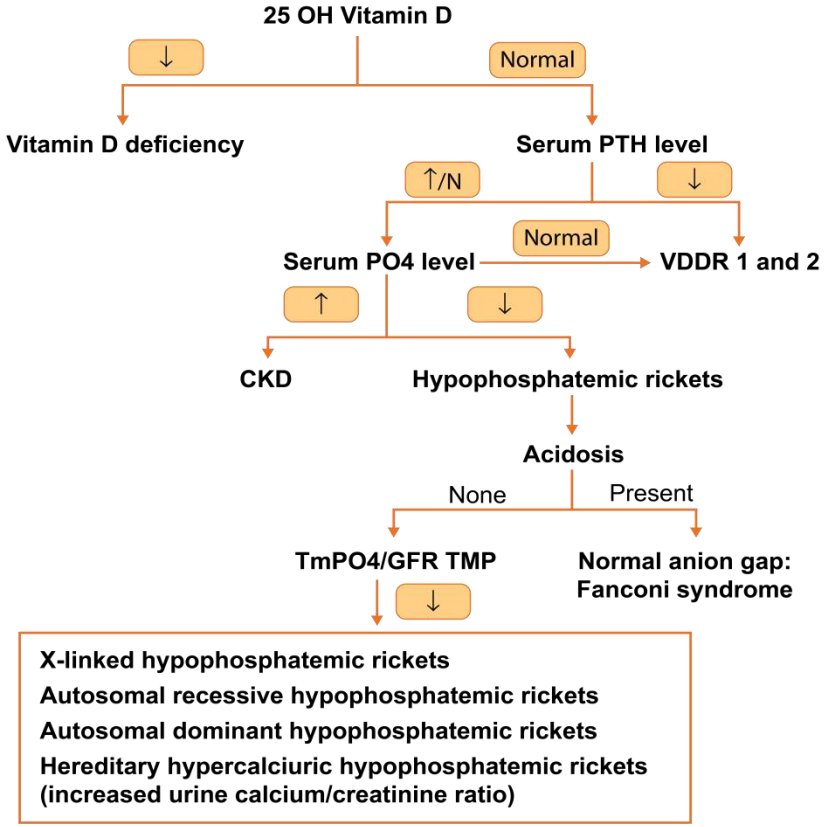
Risk Factors for Vitamin D Deficiency

Risk factors for vitamin D deficiency[1,2]	
• Fat malabsorption	• Women using sunscreen lotions
• Use of anticonvulsants	• Living in urban areas
• Chronic kidney disease	• Limited sun exposure
• Obesity	• Northern latitudes (especially in winter or spring)
• Elderly women	• Extensive clothing cover
• Dark-skinned people	• Malabsorptive syndromes (cystic fibrosis, cholestatic liver disease, and inflammatory bowel disease)
• People from areas with a thick layer of ozone	

1. Khadilkar SS. *J Obstet Gynaecol India.* 2013;63(3):147–150.
2. Mulligan ML, *et al. Am J Obstet Gynecol*. 2010;202(5):429.e1–429.e4299.

Algorithmic Approach to a Child With Rickets

Algorithmic approach to a child with rickets



Chanchlani R, *et al. Kidney Int Rep.* 2020 Apr 11;5(7):980-990.

Salient features of different types of rickets

Type	Calcium	Phosphorus	Alkaline phosphatase	PTH	25 (OH)D	1,25 $(OH)_2$ D
Calcipenic rickets						
Vitamin D deficiency	↓ or N	↓ or N	↑ or ↑↑	↑	↓	Variable
Vitamin D–dependent rickets type I	↓	↓ or N	↑↑	↑	N	↓
Vitamin D–dependent rickets type II	↓	↓ or N	↑↑	↑	N	N or ↓
Phosphenic rickets						
Nutritional phosphate deficiency	↑ or N	↓	↑ or ↑↑	↓ or N	N	↑
X-linked hypophosphatemic rickets	N	↓	↑	N or slightly ↑	N	N or ↓
Autosomal dominant hypophosphatemic rickets	N	↓	↑	N	N	↓
Autosomal recessive hypophosphatemic rickets	N	↓	↑	N	N	↓
Hereditary hypophosphatemic rickets with hypercalciuria	N	↓	↑	N or ↓	N	↑

25 (OH)D: 25-hydroxy vitamin D; 1,25 (OH)2 D: 1,25 dihydroxy vitamin D; N: Normal levels; PTH: Parathyroid hormone; ↑: Increased levels; ↓: Decreased levels.

CKD: Chronic kidney disease; GFR: Glomerular filtration rate; N, Normal; PTH: Parathyroid hormone; TMP: Renal threshold phosphate concentration; TmPO4: Renal tubular reabsorption of phosphate; VDDR: Vitamin D–dependent type 1 rickets; 25 (OH)D: 25-hydroxy vitamin D; 1,25 (OH)2 D: 1,25 dihydroxy vitamin D; N: Normal levels; PTH: Parathyroid hormone; ↑: Increased levels; ↓: Decreased levels.

Section 3:

Prevention of Rickets and Vitamin D Deficiency in Healthy Infants and Children

Sunlight Exposure

Factors that make it very difficult to determine what is the adequate sunshine exposure for any given infant or child are:

Decreased sunlight exposure during the winter and other seasons.

Lifestyle or cultural practices that decrease time spent outdoors or increase the amount of body surface area covered by clothing when outdoors further limit sunlight exposure.

Individuals with darker skin pigmentation and the use of sunscreens.

Gartner LM, *et al. Pediatrics.* 2003 Apr;111(4 Pt 1):908-10.

.

Breastfeeding and Vitamin D

Breastfed infants who do not receive supplemental vitamin D or adequate sunlight exposure are at an increased risk of developing vitamin D deficiency or rickets.

Human milk typically contains a vitamin D concentration of 25 IU/L or less.

Supplementation should begin within the first 2 months of life.

Gartner LM, *et al. Pediatrics.* 2003 Apr;111(4 Pt 1):908-10.

.

Formulas and Vitamin D

Most of the formulas actually have at least 400 IU/L.

Thus, if an infant is ingesting at least 500 mL per day of formula (vitamin D concentration of 400 IU/L), he or she will receive the recommended vitamin D intake of 200 IU per day.

Gartner LM, *et al. Pediatrics*. 2003 Apr;111(4 Pt 1):908-10.

.

Vitamin D Supplements

If the intake of vitamin D-fortified milk or formula is less than 500 mL per day, a vitamin D supplement can be provided by currently available multivitamin preparations containing 400 IU of vitamin D per mL or tablet.

It is important that special efforts be directed toward supplementing populations at increased risk of developing rickets and vitamin D deficiency, including those with increased skin pigmentation and decreased sunlight exposure.

Gartner LM, *et al. Pediatrics*. 2003 Apr;111(4 Pt 1):908-10.

.

Section 4:
Guideline Recommendations and Treatment Strategies for Vitamin D Deficiency

Vitamin D Supplementation in Indian Children: IAP Recommendations (1/3)

The IAP guidelines have recommended daily vitamin D supplementation in doses of 400 IU up to 1 year of age and 600 IU from 1 to 18 years of age.

Age	Vitamin D				Calcium		
	Prevention	*Tolerable upper limit	Treatment	Treatment with large dose (oral route preferred)	Prevention	*Tolerable upper limit	Treatment
Premature neonates	400 IU/day	1000 IU/day	1000 IU/day	NA	Intake of 150 to 220 mg/kg per day	1000 mg/day	Maximum of 175–200 mg/kg/day
Neonates	400 IU/day	1000 IU/day	2000 IU/day[$]	NA	200 mg/day	1000 mg/day	500 mg/day
1–12 months	400 IU/day	1000–1500 IU/day	2000 IU/day[$]	60000 IU weekly for 6 weeks (over 3 mo of age)	250–500 mg/day	1000–1500 mg/day	500 mg/day
1–18 years	600 IU/day	3000 IU day till 9 years, 4000 IU/day from 9 to 18 years	3000/–6000 IU/day[$]	60000 IU weekly for 6 weeks	600–800 mg/day	2500 mg/day till 8 years and 3000 mg/day for 9–18 years	600–800 mg/day
At-risk groups	400–1000 IU/day	As per age group	As per age group	As per age group	As per age group	As per age group	As per age group

[$]For a minimum of 3 months; after treatment, daily maintenance doses need to be given; *Tolerable Upper Limit - the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans.

Khadilkar A, *et al*. *Indian Pediatr*. 2017;54(7):567-573.

Vitamin D Supplementation in Indian Children: IAP Recommendations (2/3)

Preterm neonates

- Routine measurement of serum 25(OH)D levels in premature infants is not recommended; however, in the presence of a likely impairment of 25-hydroxylation, measurement of serum 25(OH)D level may be considered.

Neonates and infants up to 1 year of age

- Breastmilk is not an adequate source of vitamin D; 400 IU of vitamin D has been shown to maintain serum 25(OH)D concentrations at >50 nmol/L in breastfed infants.
- For all newborns, 400 IU of vitamin D supplementation is recommended till 1 year of age; it is also recommended that supplementation be started in the first few days of life.

Khadilkar A, *et al*. *Indian Pediatr*. 2017;54(7):567-573.

Vitamin D Supplementation in Indian Children: IAP Recommendations (3/3)

Children older than 1 year and adolescents

- All children and adolescents be supplemented with 600 IU of vitamin D that is believed to maximize bone health.
- It is recommended that adequate amounts of calcium, i.e., 600–800 mg/day, should also be supplemented/derived from dietary sources; this may be obtained from 2–3 servings of milk and milk products/day (as per recommendations from the ICMR).

At-risk groups

- In children at high risk of vitamin D deficiency, higher doses of vitamin D may be required to ensure adequate concentrations of vitamin D.
- For at-risk infants, 400–1000 IU/day, and from 1 year onward, 600–1000 IU/day may be required to maintain 25(OH)D concentrations above 50 nmol/L.

Khadilkar A, *et al*. *Indian Pediatr*. 2017;54(7):567-573.

AAP Recommendations on Vitamin D Supplementation

All infants, children, and adolescents should receive a minimum of 400 IU of vitamin D daily through diet or supplements.[1,2]

AAP has increased the recommended intake of vitamin D for infants <1 year of age from 200 to 400 IU daily with the primary intention of preventing rickets.[2]

Comparison of selected pediatric recommendations for vitamin D maintenance and treatment of deficiency[1]

SORT: KEY RECOMMENDATIONS FOR PRACTICE		
Clinical recommendation	**Evidence rating**	**Comments**
Infants ingesting less than 1 L (33.8 fl oz) of formula per day, as well as all breastfed or partially breastfed infants, should receive 400 IU of supplemental vitamin D daily.	C	Based on disease-oriented evidence and expert opinion
Children and adolescents consuming less than 1 L of vitamin D–fortified milk per day should receive 400 IU of supplemental vitamin D daily.	C	Based on disease-oriented evidence and case series
Limiting sunlight exposure may predispose children to vitamin D deficiency.	C	Based on disease-oriented evidence and expert opinion
The best available biomarker of vitamin D status is serum 25-hydroxyvitamin D levels.	C	Based on consensus and disease-oriented evidence
Children at increased risk of vitamin D deficiency may require higher dosages of supplemental vitamin D.	C	Based on disease-oriented evidence and expert opinion
A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, diseaseoriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.		

1. Casey CF, et al. *Am Fam Physician.* 2010;81(6):745–8.
2. Simon AE, et al. *Pediatrics.* 2020;145(6):e20193574.

AAP: American Academy of Pediatrics

ESPGHAN Recommendations on Vitamin D Supplementation

The ESPGHAN recommends a total daily vitamin D intake (from all sources) of 400 IU/day for infants and 600 IU/day for children and adolescents. The other recommendations include:

- Preterm infants on PN should receive 200–1000 IU/day (or 80–400 IU/kg/day) of vitamin D, term infants up to 12 months of age 400 IU/day (or 40–150 IU/kg/day), and older children 400–600 IU/day.
- Pediatric patients receiving long-term PN should be monitored periodically for vitamin D deficiency. In patients with 25(OH) vitamin D serum concentrations <50 nmol/L, additional supplementation with vitamin D should be provided.
- Oral supplementation of vitamin D should be considered in patients on partial PN as well as during weaning from PN.

Bronsky J, *et al. Clin Nutr.* 2018;37(6 Pt B):2366–2378.

ESPGHAN: European Society for Paediatric Gastroenterology Hepatology and Nutrition; PN: Parenteral nutrition .

Children Who May Need Vitamin D Supplementation

Exclusively breastfed infants or infants consuming <1000 mL of infant formula/day

Children residing north or south of the 33° latitudes or in urban/polluted environments

Children who are obese, deeply pigmented or, for cultural reasons, cover their skin with clothing

Children who are institutionalized, hospitalized, or attend schools that limit outside play

Weydert JA. *Children (Basel).* 2014;1(2):208–26.

Section 5:

Efficacy of Vitamin D Supplementation: Clinical Evidence

Single Intramuscular vs. Staggered Oral Dose of 600,000 IU Vitamin D in the Treatment of Nutritional Rickets

Objective

Comparison of efficacy and safety of two different regimens of vitamin D—600,000 IU as a single intramuscular dose and 60,000 IU orally once a week for 10 weeks—in the treatment of nutritional rickets.

Study design

- Randomized, controlled trial.
- Children with nutritional rickets (age: 0.5–5 years, n=61) were randomized to receive either 60,000 IU vitamin D orally once a week for 10 weeks or 600,000 IU of single intramuscular injection.

Endpoints

- Serum calcium, phosphate, alkaline phosphatase, urinary calcium/creatinine ratio, serum 25-hydroxy vitamin D, and radiological score were compared at 12-week follow-up.

Mondal K, *et al. J Trop Pediatr*. 2014 Jun;60(3):203-10.

.

Efficacy of the Two Treatment Regimens

Comparison of biochemical parameters in the two treatment groups

Assessment points	S. ALP (IU/L)		p-value (oral vs. I/M)	S. total calcium (mg/dL)		p-value (oral vs. I/M)	S. ionic calcium (mg/dL)		p-value (oral vs. I/M)	S. phosphate (mg/dL)		p-value (oral vs. I/M)
	Oral group n=34	I/M group n=37		Oral group n=34	I/M group n=37		Oral group n=34	I/M group n=37		Oral group n=34	I/M group n=37	
Baseline*	823.13±373.07	946.77±486.50	0.27	8.78±1.07	8.75±1.06	0.90	4.22±0.66	4.39±0.47	0.28	2.89±0.97	2.99±0.94	0.68
Day 3					8.98±0.93			4.389±0.345				
Day 7	819.06±534.26	899.87±458.32	0.87	9.42±0.81	9.65±0.78	0.27	4.49±0.28	4.53±0.27	0.6	3.97±1.07	3.91±0.99	0.81
4 weeks	378.90±334.43	366.80±245.69	0.87	10.06±0.64	9.97±0.96	0.66	4.55±0.34	4.71±0.18	**0.02**	4.59±0.94	4.56±0.95	0.92
12 weeks	204.60±101.70	199.83±106.91	0.86	10.46±0.49	10.49±0.51	0.76	4.77±0.13	4.76±0.14	0.78	4.82±0.76	4.97±0.75	0.44

*Intragroup comparison at various assessment points (only significant values are reported):
Serum ALP: p-value: 4 weeks vs. baseline <0.001 and 12 weeks vs. 4 weeks <0.001 in both the groups.
Serum calcium (total): p-value: Day 7 vs. baseline <0.001 in both groups, 12 weeks vs. 4 weeks <0.001 in both groups.
Serum ionic calcium: p-value: oral group: Day 7 vs. baseline 0.013, 4 weeks vs. Day 7 0.163 and 12 weeks vs. 4 weeks 0.001; I/M group: Day 7 vs. baseline 0.063, 4 weeks vs. Day 7 <0.001 and 12 weeks vs. 4 weeks 0.186.
Serum phosphate: p-value: Day 7 vs. baseline and 4 weeks vs. Day 7 <0.001 in both the groups, 12 weeks vs. 4 weeks 0.05 in the I/M group and 0.1 in the oral group.
Figures in bold indicate statistical significance.

ALP: Alkaline phosphatise; I/M: Intramuscular; S:Serum

Mondal K, *et al. J Trop Pediatr*. 2014 Jun;60(3):203-10.

Biochemical Features Suggestive of Rickets: No Significant Differences in Both the Groups

Number (%) of children with biochemical parameters suggestive of rickets in the two treatment groups

Number (%) of children with biochemical parameters suggestive of rickets in the two treatment groups									
Assessment points	% Children with hypocalcemia (ionic calcium <4.48 mg/dL)		p-value (oral vs. I/M)	% Children with hypophosphatemia (serum phosphate <3.8 mg/dL)		p-value (oral vs. I/M)	% Children with elevated ALP (>420 IU/L)		p-value (oral vs. I/M)
	Oral group (n=30)	I/M group (n=31)		Oral group (n=30)	I/M group (n=31)		Oral group (n=30)	I/M group (n=31)	
Baseline	13 (43.33%)	11 (35.48%)	0.27	25 (83.33%)	23 (74.19%)	0.19	25 (83.33%)	28 (90.32%)	0.21
At 7 days	6 (20%)	9 (29.03%)	0.21	17 (56.67%)	15 (48.39%)	0.26	24 (80%)	27 (87.09%)	0.23
At 4 weeks	5 (16.67%)	1 (3.23%)	**0.04**	7 (23.33%)	7 (22.58%)	0.47	10 (33.33%)	8 (25.80%)	0.26
At 12 weeks	0%	0%		1 (3.3%)	0 (0%)	0.15	1 (3.33%)	2 (6.45%)	0.29
Figures in bold indicate statistical significance.									

ALP: Alkaline phosphatise; I/M: Intramuscular; S:Serum

Mondal K, *et al. J Trop Pediatr*. 2014 Jun;60(3):203-10.

.

Significant Fall in the Mean Radiological Score

Comparison of radiological score between the two treatment groups

Comparison of radiological score between the two treatment groups						
Assessment points	**Mean radiological score**		**p-value (oral vs. I/M)**	**% of children with radiological score >1.5**		**p-value (oral vs. I/M)**
	Oral group	**I/M group**		**Oral group**	**I/M group**	
Baseline*	7.12±2.07	8.04±2.21	0.95	30 (100%)	31 (100%)	
4 weeks	4.36±1.766	3.61±1.40	0.69	29 (96.67%)	29 (93.55%)	0.29
12 weeks	0.58±0.63	0.56±0.54	0.90	1 (3.3%)	1 (3.23%)	0.49
*Intragroup comparison: p-values for mean radiological score: 4 weeks vs. baseline <0.001 and 12 weeks vs. 4 weeks <0.001 in both the groups.						

There was a significant fall in the mean radiological score after 4 and 12 weeks in both groups.

Mondal K, *et al. J Trop Pediatr*. 2014 Jun;60(3):203-10.

.

Safety of the Two Treatment Regimens: Conclusion

Mean U-Ca/Cr was 0.37+0.35 in the oral group and 0.4+0.44 in the I/M group at baseline.

No child developed hypercalciuria after starting of treatment during the study period.

A dose of 600,000 IU vitamin D administered through the oral or the intramuscular route is effective and safe in the treatment of nutritional rickets.

U-Ca/Cr: Urinary calcium/creatinine ratio; I/M: intramuscular

Mondal K, *et al. J Trop Pediatr*. 2014 Jun;60(3):203-10.

Prevention of Vitamin D Deficiency in Infancy: Daily 400 IU Vitamin D Is Sufficient

Objective

In 2005, a nationwide prevention program for vitamin D deficiency was initiated, recommending 400 IU vitamin D per day. This study was designed to evaluate the efficacy of the prevention program.

Study design

- 85 infants were recalled as part of the national screening program for congenital hypothyroidism between February 2010 and August 2010 and were evaluated in terms of their vitamin D status as well.
- All babies had been provided with free vitamin D solution and recommended to receive 400 IU (3 drops) daily.

Endpoints

- Information regarding the age at start of supplementation, the dosage, and compliance was obtained from the mothers with face-to–face interview.
- Serum 25-hydroxy vitamin D (25-OH-D), alkaline phosphatase (AP), and parathormone (PTH) levels were measured.

Mutlu GY, et al. *Int J Pediatr Endocrinol*. 2011;2011(1):4. .

Prevention of Vitamin D Deficiency With Daily 400 IU Vitamin D: Outcome

90% of cases (n=76) were receiving 3 drops (400 IU) vitamin D3 per day as recommended

70% of cases (n=59) were given vitamin D3 regularly, and the remainder had imperfect compliance

No subject had clinical signs of rickets

The mean 25-OHD level was 42.5±25.8 (median: 38.3) ng/mL.

The results of the current study suggest that daily vitamin D supplementation of 400 IU is sufficient to establish serum 25-OH-D levels >20 ng/mL (vitamin D sufficiency) in great majority of infants if they receive it regularly.

Mutlu GY, et al. *Int J Pediatr Endocrinol*. 2011;2011(1):4. .

Section 6:

Case Report: An Infant With Severe Vitamin D Deficiency Rickets Manifested as Hypocalcemic Seizures

Case Study : Presentation (1/4)

Case presentation

A six-month–old male infant was admitted with recurrent generalized afebrile seizures and was unconscious for the past 1–2 days.

Medical, personal, and family history

Infant birth history:

- Full-term infant with birth weight of 2700 g and length of 51 cm.
- Infant was delivered through normal delivery with an Apgar score of 7/9 and had cried immediately at birth.
- After birth, the infant had been formula-fed for 2 months and then given full-fat cow's milk and complementary food till around 5 months of age.
- Infant had not been having any additional daily intake of vitamin D supplements.
- At the time of hospital admission, the infant weighed 6500 g and his length was 60.5 cm.

Antenatal:

- First and second trimesters had been uneventful.
- No maternal history of diabetes mellitus or hyperparathyroidism. No history of drug intake.

The infant's parents were healthy and young, with lower level of educational attainment.

Case Study : Clinical Assessment (2/4)

Clinical assessment

The infant showed characteristic rachitic signs, such as widely open anterior fontanelle, craniotabes, chicken breast, and a large abdomen.

- Oxygen saturation (SpO_2) was 97%.
- Pulse volume was normal.
- Echocardiography and computerized tomography (CT) of the brain were normal.
- Wrist X-ray showed typical signs of rickets.

Laboratory findings

Parameter	At admission	Normal values
Free calcium	0.46 mmol/L	1.15–1.36 mmol/L
Total calcium	1.12 mmol/L	2.02–2.65 mmol/L
Phosphorus	1.01 mg/dL	0.80–1.90 mg/dL
Alkaline phosphatase	678 U/l	34–104 U/l
Parathyroid hormone	187 pg/mL	8–76 pg/mL
Serum 25(OH)D level	<7 ng/mL	20–40 ng/mL
Urine calcium–creatinine ratio	0.18	<0.2

In addition, mild anemia (hemoglobin, 10.6 g/dL) was also detected in the infant.

Case Study : Diagnosis and Treatment (3/4)

Diagnosis

Severe deficiency of vitamin D rickets with hypocalcemic seizures.

Course of treatment

The infant was given an infusion of 2 mL/kg of 10% calcium gluconate at a rate of 0.5 mL/min along with oral 2000 IU of vitamin D3 daily.

Treatment given at discharge

At the time of discharge, the infant was seizure-free and the infant was conscious.
In order to fully stabilize, the infant was prescribed 2000 IU of vitamin D3 daily and standard cow's milk-based formula. Calcium gluconate (80 mg/kg daily) was given orally over a period of 2 weeks.
Simultaneously, anemia was also corrected with oral supplements of iron. The parents were asked to bring the infant for a follow-up after 15 days.

Follow-up after 15 days

- Infant was stable with significant improvement in symptoms.
- There were no seizures and the electroencephalogram was also normal.
- Calcium levels improved to 1.89 mmol/L and serum 25-hydroxycholecalciferol levels improved to 12 ng/mL.
- The parents were advised to continue the same dose of calcium and vitamin D3 supplements for the infant and return for a follow-up after 1 month.

25(OH)D: 25-hydroxycholecalciferol

Case Study 1: Follow-up (4/4)

Follow-up after 1 month

- The infant was completely stabilized, and no seizure was observed.
- There was rapid improvement in laboratory parameters (calcium levels improved to 2.34 mmol/L and serum 25-hydroxycholecalciferol D to 28 ng/mL).
- Radiological and clinical findings of rickets also improved significantly.
- However, the parents were asked to continue with 2000 IU of vitamin D3 supplement for the infant, daily for one more month, followed by 400 IU daily till the end of the first year.

Discussion Questions

Rickets of prematurity is associated with :

a) Hypocalcemic convulsions
b) Use of frusemide diuretic
c) Vitamin D deficiency in the mother
d) All of the options given are correct

When should parents see a doctor if their children are at risk of vitamin D deficiency?

According to guidelines, what is the recommended vitamin D supplementation dose for children?

Key Messages

- Underprivileged toddlers who were deprived of sunlight had a much greater incidence of hypovitaminosis D and frank rickets.
- Nutritional rickets is the most common form of bone disease, primarily affecting infants and young children.
- The recent Indian Academy of Pediatrics (IAP) guidelines recommended daily vitamin D supplementation in doses of 400 IU up to 1 year of age and 600 IU from 1 to 18 years of age.
- A dose of 600,000 IU vitamin D administered through the oral or the intramuscular route is effective and safe in the treatment of nutritional rickets.
- Daily vitamin D supplementation of 400 U is sufficient to establish serum 25-OH-D levels >20 ng/mL (vitamin D sufficiency) in a great majority of infants if they receive it regularly.

Thank You