Name:- Dr BD Bhatia
Qualification:- MD, DCH, FIAP, FICN, FAMS, FNNF
Current Designation:- Professor and Head Pediatrics, Heritage Institute of Medical Sciences, Varanasi
President elect NNF
Experience: Working in the field of Neonatology for more than 3 decades.
Research Work and Publications: Published more than 200 papers in the field of Neonatology
25 chapters in books and monographs

Awards and Recognitions
James Flett Gold Medal, Dr. V. Balagopal Raju Gold Medal, Dr. S.S. Manchanda Gold Medal, Smt. Suraj Kali Jain Award, Dr. S.S. Manchanda Gold Medal, Sir Shri Ram Memorial Award, Dr. J.S. Bajaj Award, Award for Excellence, UP NNF Gold Medal: 2003, 2004, 2005, 2006, 2007,
Prof. A M Sur Oration at Nagpur, Prof. Jaiswal Oration at Patana, UP NNF Oration
Lifetime Achievement Award UP NNF, IAP NEOCON-2014.
Heinz Fellowship of British Pediatric Association
Guest editor of Journal of Neonatology.
Osteopenia of Prematurity

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Prof.& HOD .Pediatrics,
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Varanasi
President Elect  NNF
Post Survival Challenges

Cerebral Impairment
BPD
Growth Failure
ROP
OOP
Osteopenia of Prematurity

Also known as

- Metabolic bone disease of Prematurity
- Rickets of prematurity
- Osteopathy of prematurity

- **Definition:** Postnatal bone mineralisation that is inadequate to fully mineralise bones
- Increases in severity with decreasing gestation
## Magnitude of the Problem

- **Weight <1500 g**: 23%
- **Weight <1000 g**: 55%
- **Breast Milk fed Preterms**: 40%
- **Formula fed Preterms with Ca & P supplementation**: 16%
Perinatal Bone Physiology

- Third trimester is crucial for bone mineralization (20 g Ca, 10 g P)
  - Peak accretion rate of ‘Ca’ is 120 mg/kg/day
  - ‘P’ is 60-75 mg/kg/day

MATERNAL INTAKE CRUCIAL FOR BONE GROWTH

- Placenta plays an important role in mineral transport

- Fetal activity in-utero promotes bone growth
Privileges of being term at BIRTH

- Bone volume increases significantly with gestational age

- The trabecular thickening rate - 240 times faster in fetus than postnatally

  80% of Mineral accretion occurs in 3rd trim.

  TERM skeleton has high physical density
Mineralisation process increases exponentially between 24-37 weeks.

**Step 1:** Deposition of osteoid

**Step 2:** Mineralisation

- Newly deposited unmineralised bone matrix
- Mineralised bone
- Osteoblasts
- $\text{Ca PO}_4$
Role of placenta

- Active transport by calcium pump in basal membrane maintains 1:4 maternal to fetal calcium gradient

- Placenta converts vit.D to 1,25-dihydrocholecalciferol – fundamental for transferring phosphates to fetus,

- Chronic damage to placenta will affect P transport. (Placental Dysfunction)
Fetal kicks & bone

- Regular fetal kicks against uterine wall increases osteoblastic activity.
- Inactivity in VLBW & ELBW:
  -stimulates bone resorption by osteoclasts
  -increases urinary calcium excretion,
  -prevents addition of new bone tissue

After birth there is movt but without resistance.
Post-natal bone physiology

- Physical density of bone in term newborn decreases by 30% in first six months of life due to increase in marrow cavity **without compromising bone fragility**

- In preterm it becomes crucial factor in poorly mineralised bone
Poorly efficient absorption in developing gut

along with

Low content of mineral in human milk

determine

Net reduction of calcium & phosphorus supply

postnatally
- Deficiency of ‘Ca’ and ‘P’ is the principal cause of osteopenia

- Vitamin D deficiency - less important

  except in:

  Maternal vitamin D deficiency, drugs like phenytoin and phenobarbitone
Risk factors for Osteopenia

**Multifactorial disorder**

- Prematurity
- Feeding practices:
  - Delayed enteral feeding,
  - Prolonged use of TPN,
  - Unfortified human milk
- Lack of mechanical stimulation
- Drugs: steroids, furosemide, methylxanthines
**Drugs :-**

- Stimulate osteoclast activation
- Decrease calcium absorption
- Reduce osteoblast proliferation
- Increase calcium renal excretion

**Leading to poor bone mineralisation**
Clinical manifestations

- Most infants are asymptomatic
- Age of presentation: 6-12 weeks
  - Poor wt gain, Reduced linear growth
  - Hypotonia
  - Failure to wean from ventilr: poor chest comp
  - Pain on handling due to fractures
  - Sutural diastasis, enlargement of sagital suture

- Frank Features of Rickets in advanced cases
Consequences of osteopenia

Short-term
- Prolonged ventilator dependence
- Growth failure
- Fractures

Long-term
- Short stature
Investigations

Biochemical markers
- Serum phosphorus: Low (<4mg/dl)
- Alkaline phosphatase: High (>1000-1200 U/L) N 400-600
- Serum calcium: Normal, low, high (PTH on bone)

Alkaline phosphatase
- A sum of 3 isoenzymes: Liver  Intestine  Bone (90%)
- Useful to monitor response to treatment
TRP (Tubular reabsorption of P) & PTH

High TRP (>95%) with High Ca and High calcuria:
  - Inadeq P intake

High TRP with LOW PTH:
  - P deficiency

Low TRP with High PTH:
  - Ca deficiency

Urinary Ca & P levels:

Ca > 1.2 & P > 0.4 mmol/L: Highest bone mineral accretion
Investigations... contd

- Radiological

- Standard X-rays:
  - Thin “washed-out” bones, Cortical thinning
  - Changes occur after 40% loss of bone mineral content
  - Subjective interpretation
  - Advanced disease: fractures, rickets
Fig 1- Skeletal survey of patient, demonstrating multiple fractures and generalized osteopenia
Dual energy x-ray absorptiometry (DEXA)

- Gold standard test for assessing bone mineral content.
- Noninvasive
- Use is validated in term and preterms
- Drawbacks:
  - Ionizing radiation
  - Not portable
  - Movement artifacts
Investigations.....contd

- Quantitative ultrasound (QUS)
  - Provides information on bone mineral density and structure
  - Simple, noninvasive, nonionizing, bedside test
  - Normative data available for newborns

- Quantitative computed tomography (QCT):
  Radiation exposure
Management of osteopenia

- Nutrition is both preventive and therapeutic in osteopenia

- **Prevention**
  
  The goal is to achieve intrauterine bone mineralization pattern similar to that in fetus
FACTS TO REMEMBER

- To achieve 60 – 70% of intraut. mineralization
- The best calcium to phosphorus ratio is 1.7:1
- Together with an adequate caloric (> 80 Kcal/kg/d) and protein (2.5-3 g/kg/d) intake.
With parenteral calcium, no need of calcitriol to facilitate intest. uptake. vitamin D (400 U/day) is adequate.

During TPN, the serum calcium is not a good marker of adequacy of calcium intake (since the level is maintained stable at the expense of the bone mineralization)

Adding Ca to TPN has solubility problems
The enteral administration

Factors affecting calcium bioavailability.

- Vomiting,
- large gastric aspirates,
- immaturity of the gastrointestinal mucosa
- high Ca addition to milk causes intolerance
- Vit.D status: Intestinal Ca absorption
- Solubility of calcium salts
- Quality and quantity of lipid intake
# Recommended Intakes in Preterms

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<tbody>
<tr>
<td><strong>Calcium (mg/kg/d)</strong></td>
<td>70-140</td>
<td>120-200</td>
<td>100-160</td>
<td>28 mg/dl</td>
</tr>
<tr>
<td><strong>Phosphorus (mg/kg/d)</strong></td>
<td>50-90</td>
<td>60-140</td>
<td>60-90</td>
<td>14 mg/dl</td>
</tr>
<tr>
<td><strong>Vit D (IU/d)</strong></td>
<td>800-1600</td>
<td>200-1000</td>
<td>800-1000</td>
<td>3-5 IU/dl</td>
</tr>
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Fortification of human milk

Human milk fortifiers (HMF):

One sachet contains:

- Calcium: 50 mg
- Phosphorus: 25 mg
- Vitamin D: 250 IU
- plus proteins and other micronutrients
Other approaches
- Early enteral feeding
- Calcium and phosphorus supplementation
- Vitamin D supplementation 400 IU/d
- Limit duration of TPN
- Specialized preterm formula
  - **MULTI NUTRIENT FORTIFICATION PREFERRED**
- 180–200 mL /Kg/d of human milk

  *Provide only one-third of the in utero levels*

- In formula fed infants

  calcium bioavailability (35 - 60%) is usually less than BA with human milk (70 - 80%).

  *Human milk intake promoted with fortifiers.*

  **BANKED HUMAN MILK HAS LOWER P CONTENT THAN UNBANKED HUMAN MILK**
Human milk fortifiers

- **Indications:**
  All newborns weighing below 1500 g (<2000 g)

- **When to start?**
  Enteral intake > 100 ml/kg/d

- **How much to give?**
  2-3 sachets a day

- **How long to give HMF?**
  Until term corrected age
- With Human milk fortifiers, containing highly soluble calcium the Ca retention can reach a level of 90 mg/kg/day (88% of the overall intake).

- All supplements be equally distributed over all feeds
FORTIFIERS

Benefit:
Gain in Wt., CHL, HC & BMD

Concern:
High calcium supplement of milk is associated with:
High faecal calcium,
Prolonged gastrointestinal transit time
Impaired fat absorption.

Potential risk factors for NEC
Stimulation:

Daily exercises with gentle compression and extension/flexion of both upper and lower limbs may enhance bone mineralization (5-15 min/d X 3-8 weeks improves Wt, CHL & bone mineralization)

Limiting drug exposure: Furosemide, Steroids, Methyl Xanthines
Fortifiers: Limitation

- May increases renal solute load and decreased tolerance because of increased osmolarity
- May cause hypercalcemia/hyponatremia
- Do not contain iron
- Expensive
Treatment of osteopenia

Review mineral intake

Mineral and Vitamin D supplementation

- Ca 100-160 mg/kg/d; P 60-75 mg/kg/d
- Vitamin D 400 U/day. No role of megadose of vitamin D
- Monitor serum phosphorus and alkaline phosphatase wkly
- Babies with sec. hyperparathy : Calcitrol 0.05-0.2 mcg/kg/d to supressPTH & reduce P wastg & increasg intestinal Ca & P absorption

Duration of treatment:
Continue supplementation till serum biochemistry returns normal and there is radiological evidence of bone healing
CARRY HOME MESSAGES

Can remain silent clinically
Weekly measurement  Ca,P,Alk Phosp.  
Low serum P & high Alk Phosph 
Estimate TRP, PTH 
Early enteral feeding to reduce prevalence & severity  
Maintn normocal & normophosphatemia
Carry home message

- An adequate intake of calcium, phosphorus and vit.D. is of paramount importance.
- Maternal Ca intake in third trimester crucial.
- Switch from furosemide to an anticalciuric diuretic, such as Chlorothiazide IV or PO.
- Limit the use of Aminophyllin/ Dexamethasone and wean off as soon as medically possible.
- Passive exercises in stable VLBW infants.

- Fortify human milk OR

- Use specialized Preterm formula
THANK YOU