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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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 trimest is crucial for bone mineralizn (20 g Ca, 10 g P)
  Peak accretn rate of 'Ca' is 120mg/kg/day
  'P' is 60-75mg/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

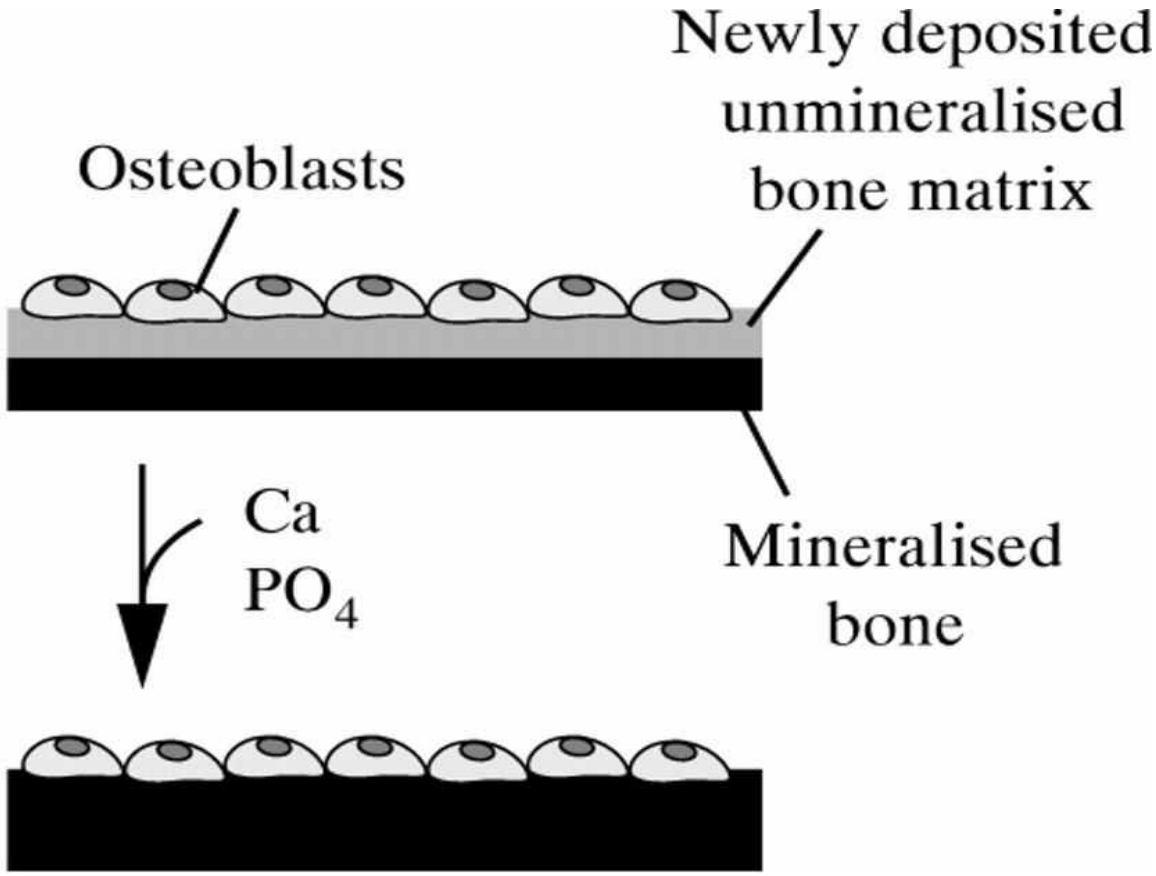
- The trabecular thickening rate - 240 times faster in fetus than postnatally

  80 % of Mineral accretn occurs in 3rd trim.

  TERM skeleton has high physicsl density

Mineralisation process increases exponentiallyB/W 24-37 weeks

Step 1:
Deposition of
osteoid



Step 2:
Mineralisation

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 transfering 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 month 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 excreation

- **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 phosphatse: 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 Highcalcuria

: 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

Investigations….contd

- 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. mineralizn
  The best calcium to phosphorus ratio

  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 of lipid intake

Recommended Intakes in Preterms

	ESPGAN (1987)	Atkinson (2005)	Rigo (2007)	Human Milk
Calcium (mg/kg/d)	70-140	120-200	100-160	28 mg/dl
Phosphorus (mg/kg/d)	50-90	60-140	60-90	14 mg/dl
Vit D (IU/d)	800-1600	200-1000	800-1000	3-5 IU/dl

Prevention…contd

- 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

Prevention…contd

- 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(<2000g)
- 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 supplemtn of milk is assoctd with:

High faecal calcium,

Prolonged gastrointestinal transit time

Impaired fat absorption.

Potential risk factors for NEC

Prevention….contd

- 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