Pediatric Osteoporosis

Approach to Diagnosis and Treatment Considerations

The Future is Bright

Egyptian Academy Bone Health & Metabolic Bone Disease
Pediatric Vs Adult Osteoporosis
Where is the difference?

**Adults:**
- BMD
- T-score ≤ -2.5 SD
- Peak Bone Mass
- Either Hip or Spine

**Children:**
- Have not yet reached PBM
- A “fracture threshold” for BMD has not been established
The 2013 International Society of Clinical Densitometry (ISCD) guidelines

- Z-score, < −2
- A clinically significant long bone fracture history ≥2 by age 10 years OR ≥3 by age 19 years

To avoid unnecessary investigations, fracture history assessed by questionnaire should be confirmed evaluating medical documentation
Pediatric Osteoporosis Diagnosis

**Adults:** BMD
- T-score < -2.5 SD peak bone mass
- Either Hip or Spine

**Children:**
- Have not yet reached PBM
- A “fracture threshold” for BMD has not been established
Pediatric Osteoporosis Diagnosis

**DXA**
- the preferred method to assess bone mass during pediatric age
- Good reproducibility
- Speed
- Reduced exposure to ionizing radiation
- Large availability of reference data

**pQCT**
- Separately analyzes trabecular and cortical bone compartments,
- Allowing the analysis of appendicular bone geometry, density, and strength,
- Enable the evaluation of fat and muscle composition of the limbs.
- However, pQCT use is still limited by:
  - The lack of standardized scanning protocols and
  - Lack normative pediatric values
Pediatric Osteoporosis: Diagnosis In Children with bone fragility:

- DXA at lumbar spine & total body less head

Skull mineralization is not affected by nutrition or environment. Skull fractures should not suggest OP.

Diagnosis of OP in paediatrics cannot be established on basis of DXA alone
Pediatric Osteoporosis: Diagnosis
Interpreting DXA measures

• DXA measures the total amount of BMC (g) contained within the skeletal region scanned and the 2-dimensional projected bone area (BA; g/cm²).

• The ration of BMC and BA expressed in units of g/cm² is referred to areal BMD (aBMD).

• DXA provides aBMD at particular skeletal site but does not allow separate assessment of these measures within the trabecular and cortical bone compartments.
Pediatric Osteoporosis: Diagnosis

DXA reporting

The terms “Osteopenia / Osteoporosis” should not appear on the Pediatric DXA reports

“Low bone mass or BMD” is the preferred term for pediatric DXA reports when aBMD Z-score is < -2.0 SD

A child can function as its own control in longitudinal follow up. Therefore DXA at the beginning of the disease is recommended.
Pediatric Osteoporosis: Diagnosis

DXA technical considerations

**DXA scans should avoid areas with metal implants, contractures or fractured vertebrae.**

There is no age limit to perform DXA scan in children. Normal values for a whole body DXA are available from the age of 3-years.

If a follow up DXA is indicated, the minimum interval between scans is 6-12 months.
Pediatric Osteoporosis

Causes of Pediatric Osteoporosis

Primary Vs secondary causes
# Pediatric Osteoporosis
## High Risk Children

<table>
<thead>
<tr>
<th>Primary bone disorders</th>
<th>Chronic inflammatory diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteogenesis imperfecta</td>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Idiopathic juvenile osteoporosis</td>
<td>Juvenile idiopathic arthritis</td>
</tr>
<tr>
<td>Osteoporosis-Pseudoglioma syndrome</td>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>Homocystinuria</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome (type I)</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>Immobility or decreased activity</td>
</tr>
<tr>
<td>GSD type 1</td>
<td>Post trauma</td>
</tr>
<tr>
<td>Juvenile/Early-onset Paget’s disease</td>
<td>Cerebral palsy</td>
</tr>
<tr>
<td>Catabolic state/Inadequate nutrition/Malabsorption</td>
<td>Spinal muscular atrophy, Muscular dystrophy</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>Medications</td>
</tr>
<tr>
<td>Malignancy - Acute lymphoblastic leukemia, Lymphoma</td>
<td>Anticonvulsant, Glucocorticosteroids, Heparin, Methotrexate (in oncology doses)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Endocrine disorders</td>
</tr>
<tr>
<td>Psychiatric eating disorders - Anorexia nervosa/Bulimia</td>
<td>Hypogonadism - Gonadal dysgenesis</td>
</tr>
<tr>
<td>Chronic malabsorption (e.g., Celiac disease)</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Acquired immunodeficiency syndrome</td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Female athlete triad disorder</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td>Delayed puberty</td>
<td></td>
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</table>
Pediatric Osteoporosis

Primary Pediatric Osteoporosis

Osteogenesis Imperfecta

- OI present with:
  - varying degrees of fracture,
  - blue sclerae,
  - dentinogenesis imperfecta,
  - ligament laxity, and
  - hearing impairment.

Idiopathic Juvenile OP

- IJO typically presents before puberty and spontaneously remits after puberty.
  - Characteristic features are:
    - bone pain,
    - walking difficulties, and
    - metaphyseal and vertebral fractures.
### Pediatric Osteoporosis

#### Secondary Pediatric Osteoporosis

<table>
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<tr>
<th>Conditions with reduced bone formation:</th>
<th>Conditions associated with high bone resorption</th>
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<tr>
<td>- Immobilization or prolonged bed rest</td>
<td>- Corticosteroid-induced bone loss</td>
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<tr>
<td>- Burn injury</td>
<td>- Juvenile Paget’s</td>
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<td>- Hepatic osteodystrophy with chronic cholestasis</td>
<td>- Primary and secondary hyperparathyroidism</td>
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<td>- Aluminum toxicity in association with total parental nutrition (TPN) or renal osteodystrophy</td>
<td>- Rickets due to vitamin D, calcium, or phosphorus deficiency</td>
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<td>- Prolonged total parental nutrition (TPN) use</td>
<td>- Idiopathic juvenile osteoporosis</td>
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<td></td>
<td>- IBD</td>
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Pediatric Osteoporosis
Conditions with low BMD for age and gender without known etiology

• Sickle cell anemia
• - Thalassemia
• - Celiac disease
• - Type I diabetes
• - Myelomeningocele
• - Long-term oral anticoagulant therapy
• - Epilepsy
• - Acute lymphoblastic leukemia
• - Cystic fibrosis
Pediatric Osteoporosis

Management Algorithm
**Who**

- 1 vertebral compression Fracture (>20% loss of height)

- Low Force – Long bone fracture
  - ≥2 long bone fractures <10-years
  - ≥3 long bones fractures Any age up to 19-years

- Children at high risk of Osteoporosis (table 1) + fracture

**Exclude**

- Other causes of fracture (e.g. rickets): Bone profile, vitamin D, X-ray wrists
- Systemic illness e.g. malignancy, inflammatory condition, neuromuscular disorders etc.

**Assess**

- DXA: aBMD > -2
  - No Fracture

- DXA: aBMD > -2 + Long bone fracture

**Consider**

- Factors to consider before treatment: Age at diagnosis of osteoporosis, pubertal status, potential for spontaneous recovery, stature, growth, pubertal development, neurological, back examination/tenderness

**DXA Scan**

- DXA: aBMD < -2 + Fracture

- Osteoporosis

- No Osteoporosis
Assess aBMD

DXA: aBMD > -2
No Fracture

No Osteoporosis

• Monitor bone health
• Spine radiograph
• Rectify/ manage risk factor
• Ensure proper nutrition
• Monitor new incidence of low force-long bone fracture

Management

DXA: BMD > -2 + Long bone fracture

Osteoporosis

Is there underlying systemic condition / risk factor?

Yes Secondary Osteoporosis

No Possible Genetic bone fragility

DXA: aBMD < -2 + Fracture
Osteoporosis

Is there underlying systemic condition / risk factor?

Yes
Secondary Osteoporosis

Possible spontaneous recover from Osteoporosis

No
Possible Genetic bone fragility

Type I collagen mutation mutation analyses

Positive: Osteogenesis Imperfecta

Negative: Genetic analyses for a mutation in one of the other bone fragility genes

Possible spontaneous recover from Osteoporosis

Yes
Sec. OP + Fr.

Min. risk factors
Nutrition
Manage secondary causes
Monitor bone health to document spontaneous recovery, including increases in BMD Z-scores appropriate for height, reshaping of vertebral fractures, absence of new non-vertebral fractures

No
Positive: Genetic Bone Fragility

Negative: Consider bone biopsy for signs of OI (hyperosteocytosis) or JO (thin osteoid seams, low bone turnover), if available

Start Treatment
Assess aBMD

DXA: aBMD > -2
   No Fracture

No Osteoporosis

- Monitor bone health
- Spine radiograph
- Rectify/ manage risk factor
- Ensure proper nutrition
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DXA: BMD > -2 + Long bone fracture

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DXA: aBMD < -2 + Fracture
Children Osteoporosis Treatment

1. Stabilization Phase (usually last for 2 years)
   Start intravenous bisphosphonate therapy with standard, published regimens (table 2) until the patient is clinically stable** (typically for a minimum of 2 years).

2. Maintenance Phase
   If risk factors resolve
   Consider discontinuation of bisphosphonate treatment once the patient is clinically stable for at least 6 to 12 months.

   Ongoing risk factors (e.g., genetic bone fragility, chronic steroid therapy):
   Consider continuing IV bisphosphonate treatment to the end of linear growth with titration to a lower dose with the goal to preserve the gains achieved during the stabilization phase and avoid over-treatment.
Osteogenesis Imperfecta

Mild
No Bisphosphonate

Still Growing?

Yes

IV Zol: 0.05 mg/kg every 6-month
(first infusion: 0.0125mg/kg)

No

Stop Zoledronate

Still Growing?

Yes

At 12-month: DXA scan
If Lumbar spine-aBMD Z-score > -2

No

Still Growing?

Yes

IV Zoledronate 0.025mg/Kg every 6-months

Still Growing?

Yes

IV Zoledronate 0.025mg/Kg every 12-months

No

Still Growing?

Yes

Still Growing?
Pediatric Osteoporosis
Secondary Pediatric Osteoporosis

**Conditions with reduced bone formation:**
- Immobilization or prolonged bed rest
- Medications: especially corticosteroids, diuretics and cyclosporine
- Burn injury
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Pediatric Osteoporosis
Treatment Outcomes

**Subjective**

-In symptomatic patients, treatment usually results in pain remittance within 2–6 weeks.

Improvement of bone and back pain

Improvement in mobility

**Objective**

- in case of vertebral fracture, healing and subsequent bone remodeling should be visible at X-ray a few months after drug administration.

- eventual reshaping of vertebral fracture

- absence of new vertebral fracture in previously normal vertebral bodies,

- absence of additional loss of vertebral height at sites of previous fractures

- Absence of new nonvertebral fractures

- to stabilize the BMD Z-score trajectory of the patient at the follow-up DXA scan.
Pediatric Osteoporosis

Treatment Outcomes: Clinical Stability

Clinically stable includes:

Absence of new VF in previously normal vertebral bodies and absence of further loss of vertebral height at sites of previous fractures.

Reshaping of vertebral fractures.

Absence of new non-vertebral fractures, bone and back pain.

Improved mobility, increases in spine BMD Z-score appropriate for height.
Clinically stable includes:

Absence of new VF in previously normal vertebral bodies and absence of further loss of vertebral height at sites of previous fractures.

Reshaping of vertebral fractures.

Absence of new non-vertebral fractures, bone and back pain.

Improved mobility, increases in spine BMD Z-score appropriate for height.
Clinical stability for 6-12 months

Treatment can be discontinued in patients whose underlying disease or risk factors resolve once they are clinically stable for 6–12 months.
Pediatric Osteoporosis

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Thank you
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Exclude
- Other causes of fracture (e.g. rickets): Bone profile, vitamin D, X-ray wrists
- Systemic illness e.g. malignancy, inflammatory condition, neuromuscular disorders etc.

Assess
- aBMD Z-score

Consider
- Factors to consider before treatment: age at diagnosis of osteoporosis, pubertal status, potential for spontaneous recovery, stature, growth, pubertal development, neurological, back examination/tenderness

DXA Scan
- DXA: aBMD > -2
  No Fracture
  No Osteoporosis ◊
- DXA: aBMD > -2 + Long bone fracture
  Osteoporosis
- DXA: aBMD < -2 + Fracture
Assess aBMD

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Is there underlying systemic condition / risk factor?

- Yes Secondary Osteoporosis
  - Possible spontaneous recover from Osteoporosis
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      - Start Treatment
    - Yes
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        - Positive: Osteogenesis Imperfecta
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  - Start Treatment