Are infants & toddlers with low body stores of Vitamin D at increased risk of suffering fragility fractures?

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The Vitamin D Study Day, 1st March 2013
Baby Jayden case renews concerns over rickets and 'child abuse' allegations

Fears grow that rising levels of vitamin-D deficiency may be leading to more cases of rickets being misdiagnosed as child abuse

Sarah Boseley and Patrick Butler
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Rohan Wray and Chana al-Alas have just had their second child returned to them by the court after she was taken into care at birth following Jayden’s death. Photograph: Sean Dempsey/PA
Jayden was an infant born to young parents of Afro-Caribbean origin

Mother not advised to take vitamin D supplements during pregnancy

He was breast fed from birth (*no vitamin D supplement*)

At age of 4½ months, referred to the University Collage Hospital, London, with a history of:

- Not crying or making any noise.
- Not opening his mouth (tongue was stuck to the roof of the mouth).
- Possibly having fits.

After admission he started to fit & his condition rapidly deteriorated.
A treating Paediatrician at UCH had queried the possibility of a metabolic bone disorder, such as rickets on CXR.

- Radiological investigations: multiple fractures, including a fracture of the skull & subdural brain haemorrhages.
- Bilateral retinal haemorrhages.
- Jayden died three days later on the PICU at GOSH.
- Coroner's PM: Pathologist noted that Jayden had low serum Ca & raised ALP. She also noted radiological features of rickets. Histology showed ‘florid rickets’.
At the conclusion of the hearing held before Mrs Justice Theis, all allegations against Jayden’s parents were found not proven.

Mrs Justice Theis concluded that Jayden’s fractures could have been caused by the day to day handling, due to fragility of Jayden's bones as a result of the his severe vitamin D deficiency rickets.

However, she concluded that the subdural haemorrhages were more likely to be caused by trauma.
This case, and the judicial analysis of the medical evidence and science given in it over the course of 4 weeks of medical and expert evidence, has serious implications for the future assessment of other vitamin D and rickets cases and may throw into doubt some findings previously made where rickets was undetected and fractures attributed to excessive force.
Questions

- Does congenital rickets exist?
- Are patients with radiological & biochemical evidence of rickets at increased risk of suffering fragility fractures?
- Can radiological changes of rickets be confused with fractures that are considered to be characteristic of NAI?
- Do infants with vitamin D insufficiency, but without radiological & biochemical evidence of rickets, have diminished bone strength?
- A couple of cases
Does congenital rickets exist?
Congenital rickets with # in infants born to osteomalacic mother from North China.

Are patients with radiological & biochemical evidence of rickets at increased risk of suffering fragility fractures?
- Review of 40 children <2 y with radiographic rickets or raised serum ALP
- 7 out of 40 (17%) had fractures
- All #s occurred in mobile children > 6 months old
- Easily distinguishable from injuries of NAI

Rickets & Fractures
VDDR Type I & Fragility Fractures

- Ca 2.06 mmol/l
- P 0.61 mmol/l (1.1 – 2.0)
- ALP 4028 IU/l (100 - 733)
- PTH 989 pg/ml (10 - 60)
- 25(OH)D 22 ng/ml
- 1,25(OH)\(_2\)D 18 pg/ml (20 - 50)

Novel inactivating mutations in the CYP27B1 gene
Fractures in under-6-month-old exclusively breast-fed infants with Rickets

<table>
<thead>
<tr>
<th></th>
<th>Reference range</th>
<th>Case 1</th>
<th>Case 2</th>
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<tbody>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.10–2.55</td>
<td>2.29</td>
<td>2.22</td>
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<tr>
<td>Phosphate (mmol/L)</td>
<td>1.2–2.2</td>
<td>0.71</td>
<td>0.97</td>
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<tr>
<td>Alkaline phosphatase (U/L)</td>
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<td>2785</td>
<td>2170</td>
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<tr>
<td>PTH (pg/mL)</td>
<td>10–60</td>
<td>520</td>
<td>428</td>
</tr>
<tr>
<td>25(OH)D (ng/mL)</td>
<td>20–50</td>
<td>2.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Severe Vitamin D & Calcium Deficiency Rickets

Ca intake ~ 150 mg/day

**Neglect!**

- **Ca:** 1.80 mmol/l (2.2 - 2.65)
- **P:** 0.76 mmol/l (1 – 1.8)
- **ALP:** 13,138 iu/l (up to 600)
- **25(OH)D:** 2.8 ng/ml (15 - 30)
- **PTH:** 1,503 pg/ml (10 - 60)
Rickets and NAI?
Cautionary tale!

Fig. 5 – Radial and ulnar metaphyseal splaying and fraying typical of rickets.
Can Radiological signs of Rickets mimic or be confused with NAI?
2 month old girl

Caucasian

Asymptomatic swollen shin

Skeletal Survey – 16 #

Mums 25OHD < 8.7 ng/ml

Infant’s 25OHD not checked.

2 month old boy
Caucasian
Swollen R Knee
Skeletal Survey – 28 #
Mums 25OHD < 4 ng/ml
2 months latter infant’s 25OHD 17.8 ng/ml.
Rickets vs. abuse: a national and international epidemic

Kathy A. Keller · Patrick D. Barnes


In summary, in infants less than 6 months of age with multiple asymptomatic metaphyseal lesions (particularly along the medial aspect of the distal femurs and proximal tibiae as well as in the distal tibiae and fibulae), pseudodias-tasis of the sutures, transverse lucencies through the forearms and ribs, and compression fractures of the spine should alert the radiologist to the possibility of osteomalacia with early metaphyseal changes, insufficiency fractures and Looser zones.
Criticisms of Keller & Barnes


- Serious misrepresentations of clinical scenarios
  - Head injuries, cervical spine injuries, multiple fractures, etc
- None of the patients had recognised signs of rickets
- Selection bias & non-disclosure of the (medicolegal) sources of their patients
- None of the children had serum 25OHD levels measured at the time they sustained injuries
- No increase in fractures in infants to accompany the vitamin D deficiency epidemic
118 < 2 year old with fractures
- 60% accidental
- 31% non-accidental
- 9% indeterminate cause

39% were vitamin D deficient or insufficient

Children with rib fractures had higher PTH
- Younger

Children with metaphyseal fractures had similar vitamin D levels to those without

Abused and non-abused children had similar vitamin D levels
Do infants with vitamin D insufficiency, but without radiological & biochemical evidence of rickets, have diminished bone strength?
In the context of unexplained fractures in infancy it is our opinion that unless there is radiological evidence of rickets using conventional X-ray techniques and biochemical evidence of rickets (i.e. abnormal blood levels of calcium, phosphate, alkaline phosphatase or parathyroid hormone) that the level of 25 hydroxyvitamin D is not relevant to the causation of the fractures.
Infants with vitamin D insufficiency, but no biochemical or radiological evidence or rickets, are not likely to be prone to fragility fractures.

However, research studies are needed to determine if these infants indeed have diminished bone strength.
Criticism of Professor’s H’s Report & Oral Evidence

(b) Similarly, Professor H ignores the mother’s formal admissions contained in her statement of January 06 which I have already recited.

(c) Critically, whilst Professor H records the results of biochemical tests taken on A’s admission to hospital he fails to comment upon any of them in his reports. It was only in cross-examination that he was finally obliged to concede that, biochemically, A’s vitamin D levels were entirely normal. In the face of that evidence he was driven to arguing that A suffered vitamin D deficiency at birth and was still so suffering when the fractures were sustained, but was recovering days later, by 20 September 2004, because she was being ‘treated’ by being fed on Cow & Gate formula milk which contains a vitamin D supplement.
a) Congenital rickets is very rare.

b) Infants with radiological & biochemical evidence of rickets are prone to fragility (pathological) fractures.

c) It should be possible to distinguish radiological changes of rickets from those that are characteristic of NAI.

d) Infants who have low body stores of vitamin D, but no biochemical or radiological evidence or rickets, are not likely to be prone to fragility fractures.

e) However, research studies are needed to determine if infants in (d) indeed have diminished bone strength.
Thank You

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