Quantitative ultrasound bone profile and vitamin D status in 5-11 years old children with intellectual disability

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Abstract
Objective: To measure serum vitamin D levels and quantitative ultrasound bone profile parameters and their correlation with each other in children with various grades of intellectual disability and bone health.

Methods: The descriptive study was conducted from January to December, 2011, at the University of Health Sciences, Lahore, Pakistan, and comprised children aged 5-11 years having intelligence quotient less than 70. Quantitative ultrasound measurements at hand phalanges were taken using an ultrasonic bone profiler. Serum calcium, phosphate and alkaline phosphatase were measured by calorimetry and 25-hydroxy vitamin D levels were measured by enzyme-linked immunosorbent assay. Data was analysed using appropriate statistical tools.

Results: Of the 61 children, 35 (57.4%) were boys and 26 (42.6%) were girls. Overall median age was 104.48 months (inter quartile range: 77.77-128.04 months). Of the total, 17 (27.9%) subjects had below normal bone profile and 51 (85%) had less than 20ng/ml 25-hydroxy vitamin D levels. A mild negative correlation of 25-hydroxy vitamin D was seen with age (p=0.006). Moderate significant correlations of amplitude dependant speed of sound were observed with age (p<0.001) and alkaline phosphatase (p<0.001).

Conclusions: Significant proportion of children with intellectual disability had below-normal bone profile. Vitamin D levels were extremely low in overwhelming majority of children with intellectual disability. Significant negative correlation of age with Vitamin D and positive correlation with amplitude dependant speed of sound may suggest increasing requirements of vitamin D with age to cope with advancing needs of growing skeleton in children with intellectual disability.

Keywords: Ad-SOS, BMD, IQ, Learning disability. (JPMA 66: 694; 2016)
to assess bone health and vitamin D status of 5-11-year-old children with ID in local population.

The current study was planned to look into the importance of early assessment of bone health and vitamin D in overall management of children with ID. Using easy-to-administer techniques for early diagnosis of musculoskeletal problems faced by underprivileged population of children to achieve targeted treatment goals and better overall health management may eventually relax the overall physical, psychological and economical limitations of caregivers and family members.

Subjects and Methods
The descriptive study was conducted from January to December, 2011, at the Department of Physiology and Cell Biology, University of Health Sciences (UHS), Lahore, Pakistan, after approval from the institutional review board. It comprised 61 children of 5-11 years of age having intelligence quotient (IQ) less than 70. Children with ID were recruited from Amin Makteb Centre for Special Education and Training, Lahore. Written informed consent was taken from parents/guardians of the children. Detailed history was taken from the parents/guardians and complete general physical and systemic examinations were conducted on each child.

Children with autistic spectrum disorders and diseases that affect bones i.e. chronic liver disease, chronic renal disease, epilepsy, primary hyperparathyroidism, hyperthyroidism, hypogonadism and diabetes mellitus, were excluded. Children regularly using drugs that affect bones i.e. steroids, anti-epileptic drugs, supplemental vitamin D and calcium were also excluded. Children with cerebral palsy (CP) were assessed using gross motor function classification system-expanded and revised and only those children were included in the study that fell within level I and/or level II. Children with ID having gross difficulties with chewing and swallowing were also excluded.

Every child in the study was also assessed by a trained psychologist. Slosson intelligence test (SIT) was used to assess the IQ of each child. Portage Early Education Programme (PEEP) was used to assess the functioning age of each child for language, socialisation, self-help, cognitive and motor skills. Quantitative ultrasound (QUS) bone profile measurements i.e. Z-score, amplitude-dependant speed of sound (Ad-SOS) and bone transmission time (BTT) were taken from distal ends of proximal phalanges of four fingers of the dominant hand using DBM Sonic Bone Profiler (IGEA, Capri, Italy, Model: BP01). Serum 25-hydroxy vitamin D (25OH(D)) level was estimated by solid phase enzyme-linked immunosorbent assay (ELISA) using automated EIA analyser (Bio-Rad Laboratories, Hercules, CA, USA) with commercially available 25OH(D) total ELISA kit (DIA source Immuno Assays S.A., Louvain-la-Neuve, Belgium). Serum calcium, phosphate and alkaline phosphatase (ALP) levels were also measured by calorimetric method using spectrophotometer (Microlab 300) with commercially available kits (Randox laboratories Ltd., Crumlin, UK).

Data was analysed using SPSS 20. For the purpose of analysis, children were further sub-grouped according to ID grades i.e. Mild ID (IQ 50 to 70), Moderate ID (IQ 25 to 30) and Severe ID (IQ 20 to 35). If the Z-Score generated by QUS was less than -2, children were classified as having below-normal bone profile. In case of normally distributed quantitative variables, mean ± standard deviation (SD), independent sample t-test, one-way analysis of variance (ANOVA) and Pearson correlation (r) were used for analysis. Non-parametric statistics i.e. Median (interquartile range [IQR]), Mann-Whitney U test, Kruskal Wallis test and Spearman's rho correlation (rho) were used for non-normally distributed quantitative variables. P < 0.05 was considered statistically significant for all purposes.

Results
Of the 61 children, 35 (57.4%) were boys and 26 (42.6%)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameter</th>
<th>Below normal bone profile</th>
<th>Normal bone profile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Median (IQR)</td>
<td>n</td>
</tr>
<tr>
<td>1</td>
<td>Bone profile Z-Score</td>
<td>17</td>
<td>-2.26 ± 1.00</td>
<td>-2.20 (-2.90–-2.00)</td>
</tr>
<tr>
<td>2</td>
<td>Ad-SOS (m/sec)</td>
<td>17</td>
<td>1759.12 ± 46.52</td>
<td>1754.00 (1724.50-1778.00)</td>
</tr>
<tr>
<td>3</td>
<td>BTT (µsec)</td>
<td>17</td>
<td>0.50 ± 0.14</td>
<td>0.48 (0.39-0.64)</td>
</tr>
<tr>
<td>4</td>
<td>25OH(D)(ng/ml)</td>
<td>17</td>
<td>11.04 ± 6.69</td>
<td>8.40 (5.29-16.76)</td>
</tr>
<tr>
<td>5</td>
<td>ALP (IU/L)</td>
<td>17</td>
<td>460.47 ± 35.53</td>
<td>460.00 (447.00-484.00)</td>
</tr>
<tr>
<td>6</td>
<td>Calcium (mg/100ml)</td>
<td>16</td>
<td>9.93 ± 0.78</td>
<td>9.96 (9.13-10.55)</td>
</tr>
<tr>
<td>7</td>
<td>Phosphate (mg/100ml)</td>
<td>16</td>
<td>4.91 ± 0.63</td>
<td>4.90 (4.40-5.43)</td>
</tr>
</tbody>
</table>

*p-value is generated by Mann-Whitney U Test. #p-value is generated by Independent Sample t-Test. *p-value ≤ 0.05 is considered statistically significant.

Ad-SOS: Amplitude dependant speed of sound. BTT: Bone transmission time. ALP: Alkaline phosphatase. 25OH(D): 25-hydroxy vitamin D.
were girls. Overall median age was 104.48 months (IQR: 77.77-128.04 months). There were 9(14.75%) children with Down’s Syndrome and 18(29.52%) with CP. The cause of ID was unknown in 34 (55.73%) children. According to ID grades, 18(29.5%) children had Mild ID, 38(62.3%) had Moderate ID and 5(8.2%) had Severe ID. Besides, 17 (27.9%) subjects had below-normal bone profile. The mean QUS bone profile Z-Score of all children with ID was -0.77±1.29. Mean Ad-SOS was 1809.26±52.54 m/sec. Ad-SOS of children with ID having below-normal bone profile was significantly lower than children with normal bone profile (p<0.001) (Figure-1B). ALP was also significantly raised in children with ID having below-normal bone profile (p<0.001).

Mean BTT of all children with ID was 0.62±0.18 μsec. BTT of children with ID having below-normal bone profile was significantly lower than that of children with normal bone profile (p=0.002). No significant difference of BTT was seen between various groups of ID (p=0.253).

Besides, 51(85%) children had below-normal 25OH(D) levels. Median 25OH(D) level of all children with ID was 8.59 (IQR: 5.46-17.87) ng/ml which was much less than the normal reference value of 20ng/ml. There was no significant difference between vitamin D levels of children with below-normal bone profile and that of children with normal bone profile (p=0.831). Also, no significant difference of Vitamin D was seen between various groups of ID (p=0.387). A mild negative correlation of 25OH(D) with bone profile was observed (Spearman’s rho= -0.499, p<0.001) (Figure-1A). ALP was also significantly raised in children with ID having below-normal bone profile (p<0.001).

### Table-2: Comparison of parameters between children in mild, moderate and severe groups of intellectual disability (ID).

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameter</th>
<th>Mild ID</th>
<th>Moderate ID</th>
<th>Severe ID</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bone profile Z-Score</td>
<td>18</td>
<td>38</td>
<td>5</td>
<td>0.369+</td>
</tr>
<tr>
<td>2</td>
<td>Ad-SOS (m/sec)</td>
<td>18</td>
<td>38</td>
<td>5</td>
<td>0.170#</td>
</tr>
<tr>
<td>3</td>
<td>BTT (µsec)</td>
<td>18</td>
<td>38</td>
<td>5</td>
<td>0.253+</td>
</tr>
<tr>
<td>4</td>
<td>25OH(D)(ng/ml)</td>
<td>17</td>
<td>38</td>
<td>5</td>
<td>0.387#</td>
</tr>
<tr>
<td>5</td>
<td>ALP (IU/L)</td>
<td>17</td>
<td>38</td>
<td>5</td>
<td>0.383#</td>
</tr>
<tr>
<td>6</td>
<td>Calcium (mg/100ml)</td>
<td>18</td>
<td>37</td>
<td>5</td>
<td>0.882+</td>
</tr>
<tr>
<td>7</td>
<td>Phosphate (mg/100ml)</td>
<td>17</td>
<td>37</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

*p-value is generated by One Way analysis of variance (ANOVA). #* p-value is generated by Kruskal-Wallis test. *p-value ≤ 0.05 is considered statistically significant.

Ad-SOS: Amplitude dependant speed of sound. BTT: Bone transmission time. ALP: Alkaline phosphatase. 25OH(D): 25-hydroxy vitamin D.
was seen with age in all children (Spearman’s rho = -0.352; p=0.006) (Figure-1C).

**Discussion**

Results of the present study show that considerable proportion (28%) of children with ID had below-normal bone mineral density (BMD) as assessed by QUS bone profile. Earlier studies have shown even greater proportion of children with disabilities having low BMD.19,20 Much less proportion of children with ID having below-normal BMD values in the present study may be explained on the basis of exclusion of children with moderate to severe motor deficits and feeding difficulties.

Significant positive correlations of Ad-SOS with age (Figure-1A) explains increase in bone mass with age in children. This finding is consistent with an earlier study21 on 50 children with genetic disorders, using the same instrument for QUS on phalanges as in the present study. The study sample showed slightly higher Ad-SOS value than our study sample which may be due to much younger children included in the present study.

Significantly higher levels of ALP in children with ID having poor bone profile when compared with ALP levels in children having normal bone profile as well as moderate negative correlation of ALP with Ad-SOS (Figure-1B) suggests increased osteoblastic activity resulting from progressive weakening of bones. This finding of raised ALP level in the present study’s sample is consistent with numerous studies done in children with poor bone health.22,23

Considerably higher proportion (85%) of children having low vitamin D levels in our study compared to previous works12,24 may be explained on the basis of already low levels of vitamin D in majority of normal local population as demonstrated by several studies done in Pakistan.9-11 The deficiency of vitamin D in children included in our study may also be explained on the basis of limited availability of foods rich in vitamin D to this underprivileged population of children. To our knowledge, the present study is the only one showing results of vitamin D assessment specifically in children with ID from Pakistan. This extreme prevalence of vitamin D deficiency of critical level in local population of children with ID is extremely important to look at for the betterment of their bone health and can be labelled as a public health concern.

A significant mild negative correlation (Figure-1C) of vitamin D with age in all children included in the current study may be explained on the basis of greater mineral and nutrient demands of growing skeleton in children. These results also suggest that pre-pubertal children already deficient in vitamin D status similar to our study population of ID children should be supplemented with higher levels of vitamin D with advancing age to achieve better peak bone mass and good skeletal growth.

Limitations of the current study are its small sample size and the lack of a comparison group of healthy children.

**Conclusions**

Significant proportion of children with ID had below-normal bone profile. Vitamin D levels were extremely low in overwhelming majority of children with ID. Significant negative correlation of age with vitamin D and positive correlation with Ad-SOS may suggest increasing requirements of vitamin D with age to cope with advancing needs of growing skeleton in children with ID.

**Disclosure:** The article or part of the article has not been submitted or published in any other journal.

Descriptive data regarding ultrasonographic bone profile of this study was presented as a part of poster at 165th Annual Conference of American Psychiatric Association (APA), Philadelphia, USA, 2012.

Descriptive data regarding ultrasonographic bone profile of the study was also presented as oral presentation at International Conference on Innovative Biological and Public Health Research (IBPHR-2014), Government College University, Lahore. MAY 6 – 8, 2014.

The results of this paper have been orally presented at 4th undergraduate & Postgraduate Research Symposium, CMH Lahore Medical College & Institute of Dentistry on 27th January, 2016 and 9th SAARC International Psychiatric Conference, Serena Hotel, Islamabad, Pakistan, 4th-6th March 2016.

**Conflict of Interest:** None.

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**References**


