SHORT COMMUNICATION

FRACTURE BURDEN IN ADULTS WITH HYPOPHOSPHATASIA

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Background
Hypophosphatasia (HPP) is an inherited metabolic disorder that is characterized by impaired skeletal mineralization and other multi-systemic effects including seizures, nephrocalcinosis, myopathy and pain. There is a spectrum of clinical severity from mortality in the infantile period to debilitating disease in other patients. HPP results from inactivating mutation(s) in the gene that encodes the tissue non-specific isoenzyme of alkaline phosphatase (TNSALP). Consequently, inorganic pyrophosphate (PPi) accumulates extracellularly and inhibits skeleton mineralization. Fractures, including atypical femoral fractures, are a complication of HPP that can cause significant morbidity, but their prevalence is not known.

Objective
Determine fracture prevalence and define the associated burden of illness for adults with HPP who first manifested HPP in childhood or in adulthood, using data acquired from two patient-reported surveys.

Study design
Following informed written consent where appropriate, two surveys, one via the internet (The HPP Impact Patient Survey [HIPS], 9/2009–6/2011) and one via telephone interview (The HPP Outcomes Study Telephone [HOST], 12/2010—3/2011), explored the impact of HPP on children and adults (i.e., > 18 yr). Study subjects were either self-selected (HIPS) or were contacted by their medical centers (HOST). Although the overall analysis included results from both children and adults, this analysis focused only on the results of adults who completed the surveys. If HPP symptoms and diagnosis first occurred > 18 yrs of age, we defined the respondent as having “adult-onset” HPP.

Results
For the overall analysis, 184 HPP patients (59 children and 125 adults) responded. For the 125 adults, the mean (SD) for self-reported fractures was 13.9 (± 22.3, range: 1 - 100). For adult-onset HPP, 43/44 (98%) experienced at least one fracture and averaged 11 (± 9, range: 1 - 30). Approximately 75% were lower extremity fractures (thigh, leg, ankle, foot, or toe). In addition, 28/44 (64%) patients required surgical fixation of a fracture. Importantly, 32% of these HPP patients modified their home as a result of HPP, and 27% employed help for physical difficulties attributed to HPP.

Conclusion
Regardless of the age of HPP onset, affected adults can sustain numerous fractures. Even those with adult-onset HPP can have fractures, indicating that HPP can impose a significant disease burden at any time.