X-Linked Hypophosphatemia (XLH) Impairs Skeletal Health Outcomes and Physical Function in Affected Adults

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INTRODUCTION
X-linked hypophosphatemia (XLH) is a rare genetic disorder of renal phosphate wasting and defective bone mineralization caused by high circulating levels of fibroblast growth factor 23 (FGF23) that impairs normal phosphate reabsorption in the kidney. Hypophosphatemia and low-normal circulating 1,25-dihydroxyvitamin D (25(OH)D) levels are typical biochemical findings. The chronic low serum phosphorus levels lead to rickets in children and osteomalacia in adults. Adults with XLH also typically experience bone and joint pain, and stiffness and may experience osteoarthritis, gait abnormalities, low-trauma fractures, and/or dental abnormalities, tibial and other lower extremity and soft tissue remains from childhood. Although much research has focused on the genetics, biochemistry, and radiologic presentation of the disease, there are no published systematic evaluations of the burden of disease and quality of life in sizeable cohorts of patients with XLH.

OBJECTIVE
To achieve a better understanding of the disease course of XLH, characterize the disease burden, and assess the disease impact on health-related quality of life in adults.

RESULTS
A total of 165 adults (127 women; 38 men) from 13 different countries completed the survey as of December 8, 2014. Adults (≥18 years old) with XLH, completed an IRB approved, online questionnaire in English. All participants were required to provide electronic consent before completing the survey. The survey includes questions on the following:

- Demographics
- Fracture history
- Current symptoms/conditions
- Medical/surgical history
- Current treatments used to manage XLH
- Use of assistive devices for walking
- Medication used to manage pain

Data collection began on June 20, 2014 and is ongoing.

CONCLUSIONS
- The majority of adults with XLH exhibit short stature and lower extremities being born structures as a consequence of unresolved rickets in childhood.
- Pain, stiffness, and gross motor impairment are prominent features of adult disease that are likely caused by progressive osteomalacia, frequent fractures, osteoarthritis, and osteoarthritis, which develops due to long-term weight bearing on misaligned joints.
- Nephrocalcinosis in adults with XLH is likely both a feature of the disease and a consequence of oral phosphate and vitamin D supplementation.
- Despite treatment with oral phosphate and vitamin D metabolite supplementation, adults with XLH experience progressively debilitating complications that significantly impact functional independence and quality of life.