SAT-244

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 (1,25[OH]$_2$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 abscesses; bowing of the lower extremities and short stature remain 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 sizable 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.

METHODS

Adults (≥18 years of age) 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
- Diagnostic history
- Medical/surgical history
- Fracture history
- Current symptoms/conditions
- Current treatments used to manage XLH
- Medication used to manage pain
- Use of assistive devices for walking
- Patient reported outcome measures (PROs) to assess pain, disability and quality of life
  - Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC®)
  - Brief Pain Inventory – Short Form (BPI-SF)
  - 36-Item Short Form Health Survey (SF-36v2)

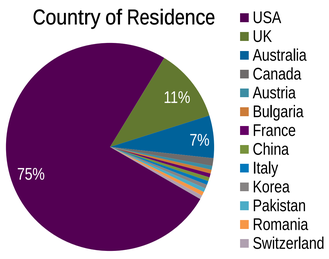
Data collection began on June 20, 2014 and is ongoing

RESULTS

A total of 165 adults (127 women; 38 men) from 13 different countries completed the survey as of December 8, 2014

Age; years	Mean	Median	Range
At survey completion	46.4	45.1	18.3 – 74.5
At first symptoms of XLH	2.6	1.0	0.0 – 50.0
At diagnosis of XLH	8.9	2.0	0.0 – 59.0

PHEX mutation confirmed	62/165 (37.6%)
US respondents	44 (71%)
Ex-US respondents	18 (29%)



Height; cm and inches	Males	Females
Mean, cm	161.3	148.6
in	63.5	58.5
Median, cm	162.6	149.9
in	64.0	59.0
Range, cm	121.9 – 182.9	115.0 – 163.0
in	48.0 – 72.0	45.3 – 64.2

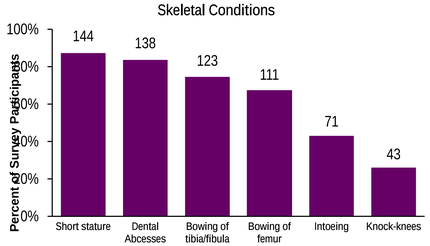
114 respondents (69%) reported current treatment for XLH	n	%
Phosphate & Vitamin D	83	72.8
Calcimimetics	8	7.0

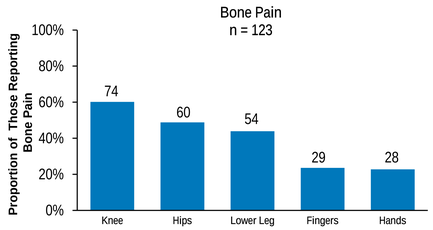
118 respondents (71%) reported taking medication for bone or joint pain at least once a week	n	%
OTC	109	65.7
Rx	36	21.7

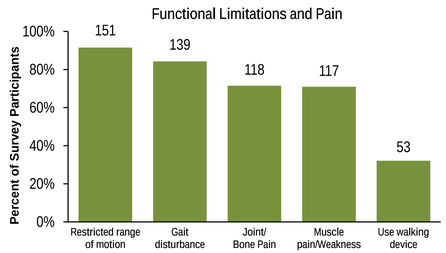
Bone fracture (ever): n = 77 (47%)	Mean	Range
Age at first fracture	26.5	3 - 63
# of fractures per person	3.7	1 - 31

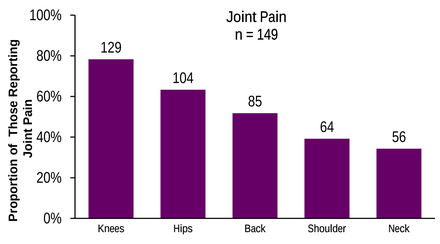
Location	n (%)	Average age at first fracture; years
Femur	31 (18.8)	29.5
Feet	26 (15.7)	37.1
Tibia/Fibula	24 (14.5)	21.5
Hip	13 (7.8)	40.0
Hand/Wrist	11 (6.6)	22.4

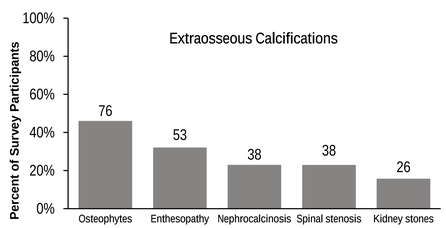
BURDEN OF DISEASE

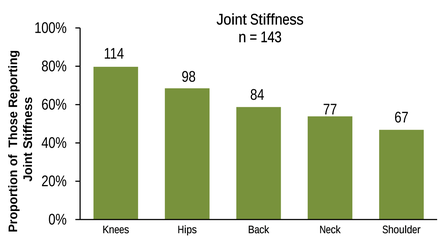












QUALITY OF LIFE

WOMAC®

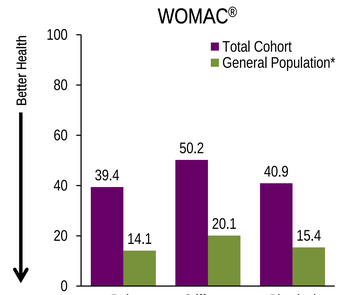
- 24-item patient-reported questionnaire developed for use in osteoarthritis
- Assesses pain (5 questions), stiffness (2 questions) and physical functioning (17 questions) over the previous 48 hours.

BPI

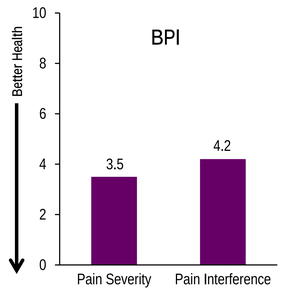
- 11-question self-reported PRO evaluating general pain
- Pain intensity (pain at its worst, least, average, and now)
- Pain interference (impact of pain on general activity, walking, work, mood, enjoyment of life, relations with others, and sleep)

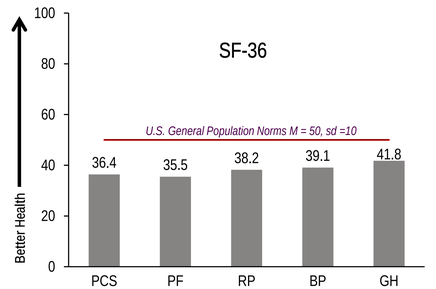
SF-36v2

- 36-question self report of functional health and well-being
- Physical Component Summary (PCS) comprises Physical Functioning (PF), Role of Limitations Due to Physical Health (RP), Bodily Pain (BP), and General Health Perceptions (GH) scales



*Cohen J. Statistical Power Analysis for the Behavioral Sciences, 2nd ed. New Jersey: Lawrence Erlbaum. 1988.





CONCLUSIONS

- The majority of adults with XLH exhibit short stature and lower extremity bowing deformities 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, extraosseous calcification, 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

Disclosures: All authors are employees and shareholders of Ultragenyx Pharmaceutical Inc., the study sponsor.

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