Subgroups of adults with X-linked hypophosphataemia: cluster analysis of patient-reported outcome measures of participants in a UK rare diseases cohort

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Abstract

Background

X-linked hypophosphataemia (XLH) is a rare genetic disorder which causes a wide range of symptoms including weakened bones and teeth. Heterogeneity of outcome groups is broadly unknown.

Aim

We set out to identify distinct subgroups of adults with XLH based on their patient-reported outcomes.

Methods

We used data from adults with XLH registered in RUDY, a UK rare diseases cohort study. We applied cluster analysis using the K-means method to seven patient-reported outcome measures (PROMs): EQ5D-5L and SF-36 physical and mental component scores (PCS and MCS), as measures of quality of life (QoL), FACIT-F of fatigue, PainDETECT and SF-MPQ-2 of pain, PSQI of sleep quality, and HADS of anxiety and depression. Instruments' scores were standardised so that all variables would be comparable. The average silhouette and elbow method were used to determine the optimal number of clusters.

Results

17 participants (76.5% females, median age 41 years) completed all seven PROMs at their first submission. Optimal number of clusters was two.

The "higher-score" cluster included 11 participants reporting higher mean QoL scores compared to the "lower-score" group (EQ5D-5L=0.817, PCS=45.40 and MCS=51.31, compared to 0.288, 19.54, and 43.44, respectively). They also reported better sleep quality (PSQI=7.64 compared to 12.67), less fatigue (FACIT-F=125.32 vs 78.00), less pain (SF-MPQ-2=1.03 compared to 3.58), and lower likelihood of being categorised with neuropathic pain (PainDETECT=5.64 vs 14.17) and depression (HADS=3.18 vs 8.17). Anxiety was found to be largely similar between clusters (HADS=6.73 vs 6.50).

Conclusions

This analysis shows that adults diagnosed with XLH report broadly heterogenous PROMs which, even with a limited sample size, allow them to be split into two very distinct subgroups, one with consistently better pain, sleep, fatigue, and depression than the other. Comparisons with other rare disease groups, other musculoskeletal conditions, and the general population would provide an important benchmark.