Exploiting Real-World Data for Early Detection of X-Linked Hypophosphatemia

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INTRODUCTION

- Rare diseases are often chronic, degenerative, and take years to be accurately identified, hindering access to therapies and proper allocation of healthcare resources.
- A paradigmatic example is **X-linked hypophosphatemia (XLH)**, a rare lifelong progressive disorder caused by mutations in the PHEX gene [1,2], characterized by excessive urinary phosphate loss and various alterations in bone mineralization [3].
- Early diagnosis of XLH is crucial for improving patients' quality of life and delaying disabling clinical outcomes. However, diagnosis is slowed down due to the rarity of the disease and the heterogeneity of clinical manifestations [4].

OBJECTIVE

Given the rarity of the disease and the resulting delayed or underdiagnosis, this study was aimed at applying a **predictive algorithm** for the early identification of subjects **potentially affected by XLH**.

PATIENTS AND METHODS

Identification of XLH predictive variables

The study was designed to test three variables identified as significant predictors of XLH in a previous analysis by our group on the administrative databases of Italian local health authorities (LHUs) covering ~13 million health-assisted and with data available from Jan-2009 to Mar-2023 [3]. These variables were searched among drug prescriptions, hospitalizations, and tests/specialist services most frequently provided to XLH-affected individuals.

Through univariate and multivariate regression models, the concomitant presence of ≥3 vitamin D prescriptions, ≥1 hospitalization for musculoskeletal diseases, ≥ 3 tests for inorganic phosphate / phosphorous was identified as predictive of XLH with an accuracy of 84% (**Fig. 1**) [3].

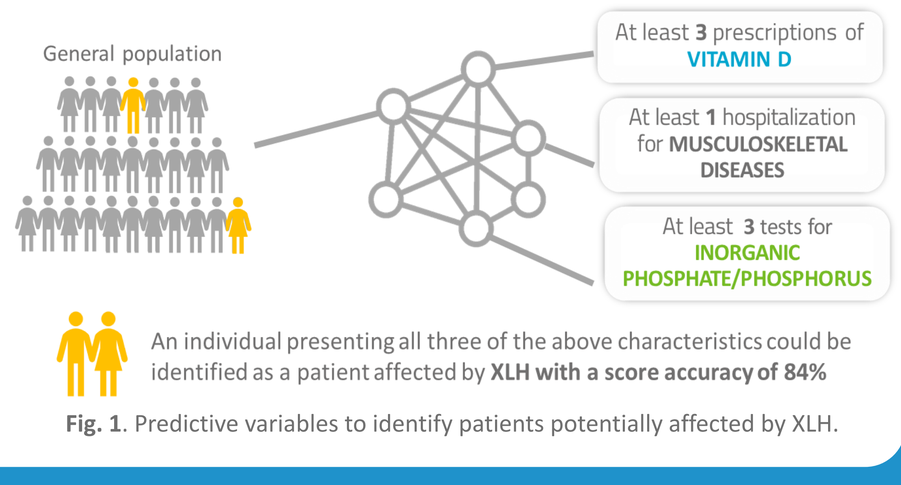

Fig. 1. Predictive variables to identify patients potentially affected by XLH.

RESULTS

- In the group of 3 LHUs under analysis, 16 patients (age 33.6 ± 22.4 years; 43.8% male) with a certain diagnosis of XLH (documented by the presence of the exemption codes RC0170 and RCG094 between Jan-2009 and Mar-2023) were identified, for an estimated prevalence of 1.3/100,000 people.
- Among the undiagnosed patients, 102 (age 23.2 ± 9.8 years; 50% male) fulfilled the criteria of the algorithm **OR** had at least 1 hospitalization for rickets and were therefore deemed as potentially affected by XLH (**Fig. 2**).
- Among them musculoskeletal and connective tissue disorders were the most common (91%), distantly followed by neurological and digestive disorders (23%). Moreover, 18% had been hospitalized for fractures, and 52% had received reimbursement for X-rays of the knees, feet or lower limbs.

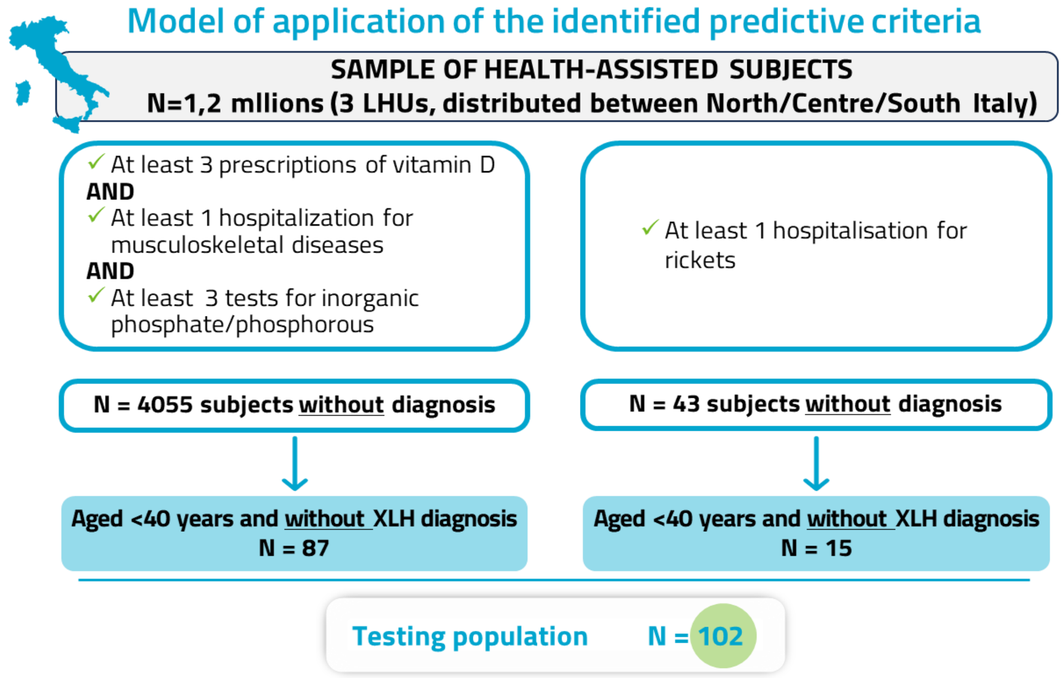

Fig. 2. Identification of patients potentially affected by XLH

TAKE-HOME MESSAGE

This model, based on a simple algorithm to identify patients potentially affected by XLH, might represent a valuable support to detect XLH and other rare diseases at an early stage, anticipating treatment, ultimately allowing a better patients' prognosis and optimization of healthcare resource allocation.

DIAGNOSIS → Algorithm to facilitate and anticipate diagnosis

CARE → Appropriate treatment to improve patients' outcomes

HEALTHCARE RESOURCES → Optimization of resource use, improved efficiency in care management

CONCLUSIONS

- In rare diseases, real-world data are essential for better understanding patient journeys and identifying patients.
- In this study, diagnostic predictors of XLH were utilized to identify patients potentially affected by the disease. Such a model can therefore be helpful to detect XLH and other rare diseases at an early stage, thus allowing more timely treatment interventions, better outcomes and optimization of healthcare resource use.
- The results of this analysis highlight the potential of applying an algorithm to reduce diagnosis times and accelerate patient care to ensure timely access to treatments.

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