Australian Paediatric Surveillance Unit

STUDY PROTOCOL

COMMENCED June 2020

X-Linked Hypophosphataemic Rickets (XLH) Prevalence Study

(A one-off survey conducted by the APSU)

BACKGROUND

X-linked hypophosphataemia (XLH) is a disorder of renal phosphate wasting, defective bone mineralisation, and impaired growth plate ossification. It is caused by inactivating mutations in the PHEX gene, and is the most common form of heritable rickets. In the absence of functional PHEX, release of fibroblast growth factor 23 (FGF23) by osteocytes is greatly increased, leading to increased loss of phosphate in the urine and consequent hypophosphatemia. FGF23 also suppresses 1,25-dihydroxyvitamin D production, resulting in decreased intestinal absorption of calcium and phosphate. Chronic low serum phosphorus levels result in defective bone mineralisation manifesting as rickets or osteomalacia.

The goal of therapy in children with XLH is to correct or minimise rickets and skeletal deformities, and to promote maximal growth potential while preventing the lifelong bone- and joint-related complications of rickets. The goal of therapy in adults is to reduce pain and optimise bone health and function.

The most common therapy for children with XLH consists of multiple daily doses of oral phosphate combined with doses of active vitamin D analogs (calcitriol). This aims to sufficiently supplement total body phosphate to allow mineralisation of bone and improve skeletal outcomes. However, supplementation therapy does not address the mechanism of urinary phosphate wasting and raises the risk of nephrocalcinosis due to increased urinary phosphate. Burosumab is a monoclonal antibody that inhibits the biological activity of FGF23, restoring renal phosphate reabsorption, increasing the serum concentration of 1,25-dihydroxyvitamin D and improving rickets and osteomalacia. The addition of Burosumab as an addition to the treatment available for children and adults with XLH emphasises the need for better understanding and identification of the condition to improve access to this treatment.

STUDY OBJECTIVES:

This study aims to:

1. Estimate the national prevalence of XLH in Australia.
2. Describe the prevalent cases in terms of:
    a. Demographics: age at diagnosis, ethnicity
    b. Family history of XLH
    c. Presenting biochemical, clinical features and complications
    d. Therapies used to treat patients with XLH

CASE DEFINITION:

Rickets during childhood: Radiological evidence of rickets, alkaline phosphatase (ALP) above the normal age and gender-matched limits of the local laboratory range and serum phosphate below the normal limits of the local laboratory range

AND

Pathogenic mutation in the PHEX gene

OR

FGF23 levels above the limits of the local laboratory range

OR

Family history that supports X-linked inheritance

REPORTING INSTRUCTIONS:

Please report any child aged < 18 years with XLH currently or previously under your care by returning the card within 1 month of receipt.

COORDINATING PRINCIPAL INVESTIGATOR

Professor Craig Munns
Department of Endocrinology and Diabetes
Children's Hospital at Westmead
Locked Bag 4001
Westmead NSW 2145
Email: craig.munns@health.nsw.gov.au

INVESTIGATORS

- Professor Elizabeth Elliott, Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead, NSW
- Dr Anne Morris, Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead, Westmead, NSW

ADVISORY GROUP

Victoria

- Dr Peter Simm, Department Endocrinology and Diabetes, The Royal Children's Hospital, Melbourne, Victoria
- Professor Peter Ebeling, Department of Medicine, Monash Medical Centre, Melbourne, Victoria
- Dr Frances Milat, Department of Medicine, Monash Medical Centre, Melbourne, Victoria

Queensland

- Professor Emma Duncan, Department of Endocrinology and Diabetes, Royal Brisbane & Women's Hospital, Brisbane, Queensland

New South Wales

- Dr Andrew Biggin, The University of Sydney Children's Hospital Westmead Clinical School, Sydney, NSW
- Associate Professor Rory Clifton-Bligh, Department of Endocrinology, Royal North Shore Hospital, Sydney, NSW
- Dr Jan Walker, Department of Endocrinology, Sydney Children's Hospital, Randwick, NSW

Western Australia

- Associate Professor Aris Siafarikas, Department of Endocrinology and Diabetes, Perth Children's Hospital, Perth, WA
- Professor Richard Prince, Faculty of Health and Medical Sciences, University of Western Australia, Perth, WA

South Australia

- Dr Sam Crafter, Department of Nephrology, Women and Children's Hospital, Adelaide, SA
- Dr Penelope Coates, Chemical Pathology, Royal Adelaide Hospital, Adelaide, SA
- Dr Elaine Tham, Department of Endocrinology and Diabetes, Women and Children's Hospital, Adelaide, SA

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