Improving the Knowledge of X-linked Hypophosphatemia among Clinicians in the Arabian Gulf and African Countries

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Rare bone disorders comprise ~5% of all rare disorders. These diverse and heterogeneous disorders are often progressive and associated with impaired mobility, chronic pain, and poor quality of life. Thus, patients often require lifelong multidisciplinary care, including medical therapies, surgeries, and the provision of aids for activities of daily living. X-linked hypophosphatemia (XLH) is one such rare bone condition. In the current issue of JDEP, Beshyah et al undertook an online survey of clinicians in the Middle East and African countries to determine their knowledge of rare metabolic bone disorders and, more specifically, about XLH. While more than 80% of respondents were aware of XLH, the survey identified significant gaps in the clinicians’ knowledge of symptoms of the condition and its management during the life course. The findings of this survey are broadly similar to those reported by Deeb et al. They undertook an online survey to determine the awareness, knowledge, and management of XLH among members of the Arab Society for Pediatric Endocrinology and Diabetes.

XLH (OMIM 307800) is the most common form of inherited rickets and osteomalacia, affecting ~1 in 20,000 to 60,000 people worldwide. It is caused by mutations in the phosphate-regulating endopeptidase homolog on the X chromosome (PHEX) gene that lead to an increase in fibroblast growth factor 23 (FGF23) levels, which causes renal phosphate wasting, reduced intestinal phosphate absorption, and low active vitamin D, ultimately resulting in chronic hypophosphatemia. It is a progressive disorder that leads to lifelong impairment of skeletal, muscular, dental, and auditory systems. It is also associated with poor quality of life in adults and increased mortality. The burden of the disease in patients with XLH progresses with age.

For more than 40 years, the treatment of XLH consisted of the administration of phosphate salts four to six times a day along with active analogs of vitamin D—calcitriol (1,25(OH)2D) or alfacalcidol (1-hydroxycholecalciferol). This is often referred to as the “conventional therapy of XLH,” which helps heal rickets and osteomalacia and improve lower limb deformities, linear growth, and dental health. However, the response to treatment is variable, and many patients are left with residual lower limb deformities requiring surgical correction. The conventional therapy is more effective in children when treatment is started early, ideally <2 years of age. Phosphate supplements have an unpleasant taste and side effects: nausea, vomiting, abdominal pains, and diarrhea. Thus, poor adherence to treatment is not uncommon, especially among adolescents. Conventional medicine is also associated with an increased risk of hypercalcemia, nephrocalcinosis, nephrolithiasis, impaired renal function, secondary hyperparathyroidism, and tertiary hyperparathyroidism.

In 2018, burosumab, a fully human monoclonal antibody that inhibits excess circulating FGF23, and thus addresses the underlying cause of the disease, was approved for the treatment of XLH in several Gulf Cooperation Council (GCC) countries. Burosumab results in sustained normalization of serum levels of phosphate, 1,25(OH)2D, and alkaline phosphatase. It also results in the healing of rickets and osteomalacia and improves growth rate and myopathy.
Early diagnosis and lifelong management of patients with XLH are essential to minimize the impact of the disease on the patient and his/her caregivers. In the absence of family history, the diagnosis of XLH is often delayed and may be confused with more common forms of rickets. An expert guideline for diagnosing and managing XLH in GCC countries has been published. Ideally, the management of patients with XLH should be undertaken by multidisciplinary teams comprising clinicians with a particular interest in bone disorders, geneticists, dentists, orthopaedic surgeons, audiologists, and physical and occupational therapists. As the burden of disease in patients with XLH progresses with age, a smooth transition from pediatric to an adult multidisciplinary bone clinic is essential.

The surveys by Beshyah et al² and Deeb et al³ have identified the critical educational needs of teams of health professionals caring for patients with XLH and rare bone disorders. Two important questions arise from these surveys:

1. How can the knowledge of XLH among clinicians in GCC and African countries be improved?
2. More importantly, how can the care of XLH patients be improved in resource-poor countries lacking diagnostic resources and specialist centers with a “critical mass” of health care professionals who can provide lifelong multidisciplinary care?

Traditional face-to-face didactic teaching in a lecture theater or attending conferences and workshops only allows educational access to those who can physically attend. The cost of travel and accommodation and visa restrictions can limit the attendance of health care professionals from low-income and middle-income countries at international meetings/conferences. One positive “side effect” of the 2019 COVID-19 pandemic was the rapid acceleration in the use of digital technologies both for scientific discourse and in improving patient care. With the global expansion of the internet and the availability of smartphone and desktop devices, digital media platforms have the potential to disseminate education and training to health care professionals in resource-poor communities. One such platform is the Rare Bone Health TeleECHO program,¹ which uses real-time videoconferencing technology as a way of training, mentoring, and ultimately empowering health care professionals about rare bone disorders, in some of the hardest-to-reach communities. Similarly, the “Tin Soldiers Continuing Medical Education Master series” provides virtual and international educational opportunities for health care professionals about fibrodisplasia ossificans progressiva, an ultra-rare bone disorder.¹⁵ Such programs would allow teams specializing in the care of patients with XLH (and other rare bone disorders) at the so-called centers of excellence to share their medical knowledge and expertise through didactic presentations and interactive discussion of anonymized cases with colleagues in low-income and middle-income countries.

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M.Z.M. is the only author who contributed to this study.

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No ethical approval is required.

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