Hypophosphatasia (HPP) is a genetic disease caused by one or more mutations in the alkaline phosphatase (ALP) gene, which encodes tissue-specific ALP and affects the mineralization process. Accordingly, arthralgia, fractures, and dental abnormalities have been reported in adults, and fatal outcomes in children. This metabolic disorder is commonly misdiagnosed with other more prevalent bone diseases due to its low prevalence and lack of recognition (i.e. chondrocalcinosis). However, no epidemiological studies on the prevalence of HPP in the rheumatological patient population have been available to date.

Objectives: To identify the prevalence of HPP in rheumatological patients screened for persistent low levels of ALP and association with mutations in the ALP gene.

Methods: All adult rheumatology patients were screened for pathological low levels of ALP (< 35 IU/L) between January 1, 2017 and June 30, 2019 at the Department of Rheumatology, Clinic of Internal Medicine III, University Hospital Bonn, Germany. Medical files of patients with pathological low ALP levels were then reviewed for clinical signs and symptoms as well as results of genetic testing for HPP (full sequencing using Next Generation Sequencing).

Results: In total, 2,289 rheumatology patients were screened for low ALP levels. In 60 patients (2.62 %), pathological low ALP levels were identified, while in 30 of these (1.31 %), persistent low ALP levels were detected. In 19 of the 30 patients, genetic tests for ALP gene mutations were done. Seven out of 19 patients (36.84 %) had HPP-related symptoms (fracture, dental abnormalities) with normal bone densitometry, while four of these patients (21.05 %) had a history of fracture and three patients (15.78 %) showed dental abnormalities. In addition to the typical HPP signs and symptoms, 13 patients (68.42 %) showed mutations in the ALP gene. One of the ALP mutations was found to be a novel genetic variant, classified as pathological. Interestingly, no association with chondrocalcinosis was detected.

Conclusion: In summary, it can be concluded that HPP is an under-diagnosed condition with a higher proportion of affected rheumatologic patients than previously thought (at least 0.56 percent of rheumatologic patients vs. 0.01 percent in a Spanish healthy population). If we replicate these numbers for the German population (83 million, 5 percent of whom suffer from rheumatic conditions) the yield is approximately 4.15 million. This possibly indicates that 23,240 potential cases of HPP are currently not diagnosed. Therefore, implementation of a protocol in clinical practice to prevent underdiagnosis of HPP and to treat this disease appropriately is essential.

REFERENCES:

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PREVALENCE OF HYPOPHOSPHATASIA IN ADULT RHUMATOLOGY PATIENTS SCREENED BY LOW LEVELS OF ALKALINE PHOSPHATASE

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Background: Hypophosphatasia (HPP) is a genetic disease caused by one or more mutations in the alkaline phosphatase (ALP) gene, which encodes tissue-specific ALP and affects the mineralization process. Accordingly, arthralgia, fractures, and dental abnormalities have been reported in adults, and fatal outcomes in children. This metabolic disorder is commonly misdiagnosed with other more prevalent bone diseases due to its low prevalence and lack of recognition (i.e. chondrocalcinosis). However, no epidemiological studies on the prevalence of HPP in the rheumatological patient population have been available to date.

Objectives: To identify the prevalence of HPP in rheumatological patients screened for persistent low levels of ALP and association with mutations in the ALP gene.

HPP patients from an adult rheumatology population. Threshold alkaline phosphatase < 35 IU/L at 37 °C. ALP: alkaline phosphatase

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