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Letter to the Editor: "Nephrocalcinosis and Nephrolithiasis in X-Linked Hypophosphatemic Rickets: Diagnostic Imaging and Risk Factors"

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We read with interest the article by Colares Neto GP et al [1] recently published in the Journal of the Endocrine Society about the risk factors that can influence the appearance of nephrocalcinosis in patients with X-Linked Hypophosphatemia (XLH). However, we have some concerns about the information provided.

First of all, nephrocalcinosis (NC) refers to calcium oxalate or calcium phosphate deposition within the kidney [2]. Therefore, it is very surprising that the patients with NC mentioned in this paper do not have any episode of hypercalciuria during treatment. If so, the authors could provide an explanation about this finding.

The authors calculated the mean values of at least 3 urinary calcium samples and other electrolytes for each patient. We do not agree with this methodology. One should consider that the urinary concentration of the electrolytes presents a wide daily variability. Thus, it would be important to know the concentration in each sample and not the average of samples [3]. Finally, collection of 24-hour urine is complicated and its accuracy should be checked with a 24-hour urinary concentration of creatinine, which was not reported [4].

Above all, the main concern is related to the conclusion that "the main metabolic risk factor for the development of NC was hyperphosphaturia." In clinical usage, the term phosphaturia is used to describe an impaired renal tubular capacity to reabsorb phosphate, leading to urinary phosphate wasting. Reabsorption of phosphate is a saturable carrier-mediated process, and the amount of phosphate excreted in urine varies according to the filtered load. This, in turn, largely reflects intake, which varies widely. Hence, unless undertaken during metabolic balance studies, measurements of 24-hour urine phosphate cannot be used to diagnose phosphaturia [5].

Therefore, to evaluate the extent of phosphaturia it is important to calculate the tubular reabsorption of phosphate (TRP) and tubular maximum reabsorption of phosphate per unit of glomerular filtrate (TmP/GFR) [5]. These parameters in the study by Colares Neto et al showed no difference between children and adults. To further investigate the possible correlation between phosphaturia and NC, the authors should have compared patients with

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and without NC by age group. In our view, the lack of these analysis weakens the conclusion of the study. Importantly, the authors' conclusion may lead to a misinterpretation that the isolated hyperphosphaturia should be considered to be the main risk factor. By the same logic, the authors conclude that hypercalciuria has no impact in NC development in XLH patients under conventional treatment. This could be a random finding with uncertain scientific meaning. The references that the authors included to support the importance of phosphaturia in NC development were based on tubular reabsorption of phosphate and TmP/GFR.

The authors implicated XLH as a disease in which patients can develop NC, based on the fact that 4 adults who did not take phosphate during childhood developed NC. However, they did not discuss prior treatment with calcitriol, which could be implicated with NC [3].

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Additional Information

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