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Development of a predictive model for FGF-23 levels in children with chronic kidney disease

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Background and Aims: The global prevalence of Chronic Kidney Disease (CKD) among the population is approximately 10%, with this rate steadily increasing. Epidemiological data on CKD in childhood are scarce and show significant variability across different countries. One of the most serious complications is mineral and bone disorders (CKD-MBD), which worsen the clinical course and prognosis of patients. The understanding of the pathogenesis of CKD-MBD has undergone substantial changes since the discovery of Fibroblast growth factor 23 (FGF-23), a 32 kDa peptide produced by osteocytes and osteoblasts, has emerged as a key regulator of phosphate metabolism. It is acknowledged that FGF-23 levels in the serum gradually increase as renal function declines, i.e., with the progression of CKD. According to various studies, FGF-23 may also be associated with cardiovascular complications, such as left ventricular hypertrophy (LVH). There is evidence indicating that FGF-23 may be regarded as an independent risk factor for mortality. Considering the predictive abilities of FGF-23 in relation to the onset of complications and mortality in children with CKD, there is a need for its assessment in serum or plasma. However, the availability of the FGF-23 assay kit in Kazakhstan is not consistently ensured in clinical practice, and its logistics may be time-consuming and financially burdensome. Therefore, we aimed to develop a predictive model to estimate FGF-23 levels based on accessible clinical and laboratory parameters.

Method: 73 children with CKD were enrolled in the pilot study. The average age was 9.79 ± 0.58 years, 52.1% males and 47.9% females. The study adhered to the principles outlined in the Declaration of Helsinki. A comprehensive evaluation of all clinical and necessary laboratory characteristics was conducted. The estimated glomerular filtration rate (eGFR) was calculated according to the Schwartz formula. FGF-23 levels were measured in serum using a multimatrix ELISA kit (Biomedica Medizinprodukte GmbH, Austria). For the development of the predictive model, we employed the decision tree learning approach. Statistical analysis and modeling were conducted using SPSS version 27 (IBM, USA).

Results: Initially, we included all clinical and laboratory parameters showing statistically significant associations with FGF-23 as independent variables and created various models. Then, we selected the most accurate predictive model which included 3 predictors: phosphate, eGFR and LVH. We found out a correlation between FGF-23 with eGFR ($r = -0{,}826$, $p = 0.000$), with phosphate ($r = 0.473$, $p = 0.000$). LVH is also associated with high FGF-23 ($p = 0.000$). At the start of the algorithm, the phosphate level should be estimated, and if it is normal, the next step is to determine eGFR. When eGFR is more than 85.7 ml/min, in 92.9% of cases FGF-23 will be within normal limits. eGFR less than 28.3 ml/min predicts a 100% chance of high FGF-23 levels. If the eGFR is in the range from 28.3 to 85.7 ml/min, the next we should determine the presence of LVH in the child. So, if a patient has been diagnosed with LVH, this indicates a high level of FGF-23 in 100% of cases. On the contrary, if the patient does not have LVH, then this probability is reduced to 52.9%. In the case of initially elevated phosphate, there is a need to evaluate if the patient has LVH or not regardless of eGFR. If it is present, the probability of a high level of FGF-23 is 100%, and if absent, it is 55.6%. Our predictive model demonstrated a high sensitivity of 98%, an overall percentage of accuracy is 82.2 ± 4.5%.

Conclusion: A decision tree algorithm based on a limited set of available clinical and laboratory characteristics such as phosphate, eGFR and LVH might be considered as a useful tool for predicting FGF-23 levels. This algorithmic approach enables the identification and evaluation of individuals with elevated FGF-23 who are at high risk for complications associated with CKD.