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Serum Fibroblast Growth Factor-23 Levels are Associated with an Increased Risk of Developing Anemia in Patients with Non-dialysis Chronic Kidney Disease

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Objectives : Fibroblast growth factor-23 (FGF23) is an established biomarker of adverse outcomes in patients with chronic kidney disease (CKD). Several cross-sectional studies have suggested possible association between FGF23 and anemia in these patients. Thus, we further explored this relationship and examined whether FGF23 level can predict the future development of anemia in a large-scale prospective cohort study.

Methods : Among 2,238 patients with non-dialysis CKD enrolled in the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD), 2,089 patients who measured hemoglobin, hepcidin, iron profiles and intact FGF23 (iFGF23) level were included in the analysis. iFGF23 and hepcidin levels were determined by commercially available enzyme-linked immunosorbent assay kits. Anemia was defined as a hemoglobin level of < 13.0 g/dL and 12.0 g/dL for male and female, respectively.

Results : The mean age was 53.6 ± 12.2 years and 1,275 (61.0%) patients were males. At baseline, anemia was found in 925 (44.3%) patients. Log iFGF23 significantly correlated with hepcidin, but inversely with iron profiles and hemoglobin. A multivariate logistic regression model showed that log iFGF23 was independently associated with anemia (odds ratio [OR], 1.15; 95% confidence interval [CI], 1.05–1.26, P=0.003). This association was particularly evident in patients younger than 55 years and patients with high inflammation or iron deficiency. Among 1164 patients without baseline anemia, 295 (25.3%) patients developed anemia during a median follow-up duration of 21 (interquartile range, 7–38) months. Anemia occurred in 63 (17.7%), 85 (24.8%), 85 (32.0%), and 62 (31.0%) patients in the 1st, 2nd, 3rd, and 4th quartile of

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iFGF23, respectively ($P < 0.001$). In the fully adjusted multivariable Cox models, risk of developing anemia was significantly higher in the 3rd [hazard ratio (HR), 1.74; 95% confidence interval (CI), 1.21–2.51; $P = 0.003$] and 4th (HR, 1.67; 95% CI, 1.11–2.53; $P = 0.02$) quartile of iFGF23 as compared to the 1st quartile. Similar association was observed in a model when iFGF23 was treated as a continuous variable.

Conclusions : We showed that high serum iFGF23 levels are associated with an increased risk of developing anemia in patients with non-dialysis CKD. Our findings suggest that serum iFGF23 levels can emerge as an independent predictor of anemia. Further studies are required to elucidate mechanism for FGF23-associated anemia in these patients.

Keywords : Fibroblast growth factor-23, anemia, chronic kidney disease