KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Oral
Abstract Submission No. : OR-1213

High blood urea nitrogen is associated with anemia development in chronic kidney disease: The results from the KNOW-CKD study

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Objectives: Blood urea nitrogen (BUN) is not only reflecting the deterioration of the renal function but is also a uremic toxin. We aimed to show the effects of BUN on anemia in CKD patients.

Methods: This prospective study included 2,196 subjects enrolled in the KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease (KNOW-CKD) between 2011 and 2016, after excluding 42 subjects without data on BUN or hemoglobin. Hemoglobin levels were measured yearly during a mean follow-up period of 37.5±22.1 months. Anemia was defined as hemoglobin <13.0 g/dL in men and 12.0 g/dL in women.

Results: Mean subjects age was 53.7±12.3 years, and 1339 (61.0%) were men. BUN level was inversely associated with estimated glomerular filtration rate (eGFR) and serum albumin, and positively associated with urine protein to creatinine ratio and Charlson comorbidity index. BUN also inversely associated with hemoglobin, iron level, and transferrin saturation. BUN was inversely associated with hemoglobin in multivariable linear regression analysis after adjustment with multiple confounders (β, -0.03; 95% confidence interval [CI], -0.04, -0.03; P<0.001). Among 1,169 subjects without anemia at baseline, 414 (35.4%) subjects newly developed anemia during a follow-up period. In multivariable Cox regression analysis, high BUN level (per 1mg/dL increase, hazard ratio [HR], 1.03; 95% CI 1.01-1.04; P<0.001) and high quartile BUN groups (3rd vs. 1st quartile; HR 1.62; 95% CI 1.10-2.39; P=0.014: 4th vs. 1st quartile; HR 2.25; 95% CI 1.38-3.69; P=0.011) were significantly associated with an increased risk of anemia development. Furthermore, the adjusted HR for incident anemia was found to be significantly increased at BUN levels of >19 mg/dL.

Conclusions: High BUN level is significantly associated with a low hemoglobin level and predicts the development of anemia in CKD patients. These findings show the potential role of BUN, as a uremic toxin, in CKD-related anemia.