# Relationship between serum inorganic phosphorus levels and cognitive decline over 2 years in older adults with pre-dialysis chronic kidney disease

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*To The Editor,*

Higher levels of serum inorganic phosphorus (iP) are associated with mortality and cardiovascular events in patients with chronic kidney disease (CKD) [1]. Abnormal phosphorus metabolism is one assumed factor of cognitive decline in these patients [2], but its relationship with iP is not reported in CKD.

In this 2-year prospective cohort study, we enrolled 134 consecutive patients aged ≥60 years undergoing outpatient treatment for pre-dialysis CKD (stage 3-5). Cognitive function was assessed at baseline and at 2-year follow-up via the Mini-Mental State Examination (MMSE). Percent change between baseline and follow-up MMSE scores (%MMSE) was calculated as (follow-up MMSE score − baseline MMSE score/baseline MMSE score) × 100. We performed a medical records review to investigate baseline demographic and clinical characteristics including age, sex, iP level, estimated glomerular filtration rate (eGFR), comorbidities (diabetes mellitus, cardiovascular disease) and absence of low physical function. We assessed the impact of iP on %MMSE with multiple regression analysis. %MMSE was the independent variable, iP the dependent variable, and covariates entered were factors affecting cognitive decline as reported in a previous study of patients with CKD [3].

Ultimately, 86 patients completed the 2-year follow-up assessment. Mean patient age was 77.7±6.7 years, and 62 (72.1%) patients were men. Mean eGFR was 30.8±11.9 mL/min/1.73 $m^2$, and the median (interquartile range) iP level was 3.4 (3.0–3.8) mg/dL. At 2 years, the MMSE score increased in 24 patients, remained unchanged in 23, and declined in 39, and the mean %MMSE was -2.2±8.2%. Multiple regression analysis for cognitive decline over the follow-up period showed iP levels to be significantly associated with %MMSE in the crude model (β: -0.27, 95% CI: -7.60 to -0.92, per 1 mg/dL). After adjustment for covariates (age, diabetes mellitus/cardiovascular disease, eGFR, baseline MMSE score and low physical function), iP levels were still significantly associated

with %MMSE (β: -0.22, 95% CI: -6.91 to -0.05, per 1 mg/dL).

In a previous study of US veterans, higher levels of iP, even if within normal range, were associated with increased risk of incident vascular dementia [4], and high iP levels are a cause of arteriosclerosis and endothelial dysfunction [5]. Thus, higher iP levels may lead to cognitive decline through impaired vascular function in pre-dialysis patients with CKD.

This study has an important limitation. Fibroblast growth factor 23 (FGF23) and serum 25-OH vitamin D are involved in the regulation of iP metabolism, and these factors may be related to cognitive decline. However, we did not investigate these factors in this study.

In conclusion, in older adults with pre-dialysis CKD, the iP level may affect cognitive decline, indicating that management of the iP level, even if within normal range, is of high importance.

**Compliance with Ethical Standards**

**Conflict of interest** The authors have declared that no conflict of interest exists.

**Human and animal rights** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted (IRB approval number 2691), and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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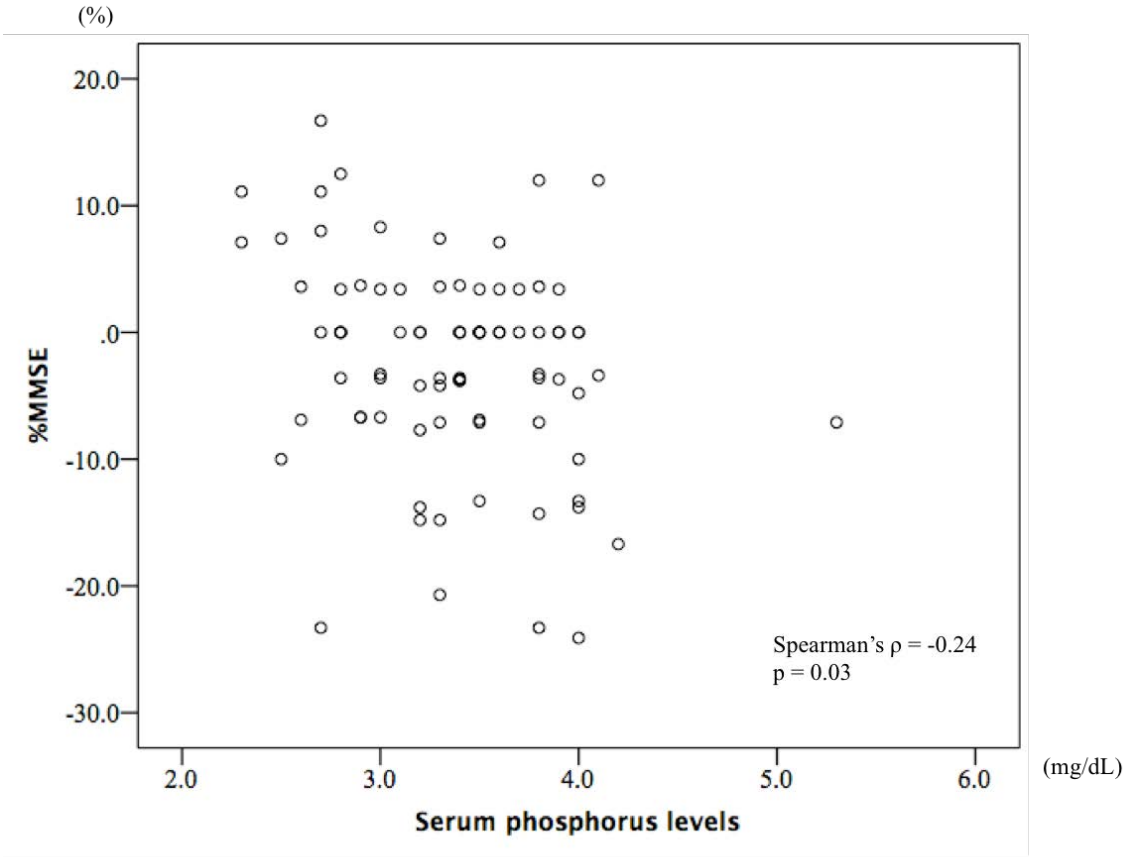


Fig. 1. Scattergram showing the relationship between serum inorganic phosphorus levels and %MMSE.
MMSE: Mini-Mental State Examination.