The relationship between vitamin D and estimated glomerular filtration rate and urine microalbumin/creatinine ratio in Korean adults

Sung Gil Kim, Gwang Seok Kim, Jun Ho Lee, Ae Eun Moon and Hyun Yoon

1Department of Radiological Science and 2Department of Biomedical Laboratory Science, Hanlyo University, 94-13 Hallyeodae-gil, Gwangyang-eup, Gwangyang-si, Jeollanam-do 57764, Korea
2Department of Emergency Medical Technology, Chungbuk Health and Science University, 10 Deogam-gil, Naesu-eup, Cheongwon-gu, Cheongju-si, Chungcheongbuk-do 28150, Korea
3Department of Biomedical Laboratory Science, Wonkwang Health Science University, 345-13 Sinyong-dong, Iksan-si, Jeollabuk-do 54538, Korea
4Department of Dental Hygiene, Honam University, 417 Eodeung-daero, Gwangsan-gu, Gwangju 62399, Korea

The present study was conducted to assess the association between 25-hydroxyvitamin D [25(OH)D], estimated glomerular filtration rate (eGFR) and urine microalbumin/creatinine ratio (uACR) in Korean adults. Data on 4,948 adults aged ≥20 years from the Korean National Health and Nutrition Examination Survey V-3 (2012) were analyzed. After adjusting for the related variables (except age), the odds ratios (ORs) of vitamin D deficiency with the normal group as a reference were significantly higher in the decreased eGFR plus elevated uACR group [3.089 (95% CI, 1.722–5.544)] but not in the elevated uACR [1.247 (95% CI, 0.986–1.577)] and decreased eGFR group [1.303 (95% CI, 0.789–2.152)]. However, when further adjusting for age, the ORs of vitamin D deficiency with the normal group as a reference were significantly higher in the elevated uACR group [1.312 (95% CI, 1.035–1.662)] and decreased eGFR [1.761 (95% CI, 1.062–2.919)] and the decreased eGFR plus elevated uACR group [3.549 (95% CI, 1.975–6.365)]. In conclusion, vitamin D deficiency was positively associated with the elevated uACR and decreased eGFR. In addition, vitamin D level decreased greatly when decreased eGFR and elevated uACR appeared simultaneously.

Key Words: vitamin D, estimated glomerular filtration rate, urine microalbumin/creatinine ratio

Chronic kidney disease (CKD) is a global public health problem with 20 million adult Americans currently living with CKD in various stages of CKD: ≥400,000 individuals with end-stage kidney disease and ≥300,000 individuals requiring maintenance hemodialysis.1–3 CKD is defined by an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m²; a decrease in eGFR is a risk factor for cardiovascular disease (CVD) and is correlated with cardiovascular mortality and morbidity in high-risk groups.4,5 Albuminuria is a well-known predictor of CKD progression and is considered to be an early sign of glomerular damage used as a risk factor for end-stage renal disease in people with diabetes mellitus.6,7

Vitamin D from the diet or dermal synthesis from sunlight is biologically inactive [25-hydroxyvitamin D, 25(OH)D], which is metabolized to the biologically active 1,25 dihydroxyvitamin D [1,25(OH)2D] through enzymatic conversion in the kidney.8,9 25(OH)D usually functions as storage due to its relatively long half-life of 2–3 weeks, and the total vitamin D status in the human body is generally estimated through measurements of serum 25(OH)D.10 Vitamin D is known to be involved in calcium and phosphate absorption in the intestines, and maintains sufficient concentrations of circulating calcium and phosphate levels and normal mineralization of bone by providing the minerals to bone-forming sites.11,12

Recently, vitamin D has received an attention on concerning its effect on CKD and CVD.13,14 It is important to monitor eGFR and the urine microalbumin/creatinine ratio (uACR) in patients with CKD and progressive CVD. In particular, when a decrease in eGFR is combined with an increase in uACR, CVD mortality rates in patients with CKD increase greatly.15 The Republic of Korea has recently become known as a country that has a severe vitamin D deficiency problem,16 and the burden of CKD and CVD are also increasing. Therefore, our objective in this study was to assess the association between vitamin D and eGFR and uACR in Korean adults using data from the fifth Korean National Health and Nutrition Examination Survey (KNHANES V-3; 2012) to be representative of the Korean population.

Methods

Study subjects. This study was performed using data from the Korean National Health and Nutrition Examination Survey (KNHANES V-3). KNHANES V-3 were each conducted for 1 year (2012), using a rolling sampling survey that involved a complex, stratified, multistage, probability cluster survey of a representative sample of the non-institutionalized civilian population in South Korea. The survey was composed of three parts: a health interview survey, a health examination survey and a nutrition survey. Each survey was conducted by specially trained interviewers. The interviewers were not provided with any prior information regarding specific participants before conducting the interviews. Participants provided written informed consent to participate in this survey, and we received the data in anonymized form. In the KNHANES V-3 (2012), 8,958 individuals over age 1 were sampled for the survey. Among them, of the 6,665 subjects who participated in the KNHANES V-3, we limited the analyses to adults aged ≥20 years. We excluded participants 1,717 subjects whose data were missing for important analytic variables, such as serum 25(OH)D, urine microalbumin and creatinine level, or various blood chemistry tests; pregnant women; and a high uACR (uACR ≥3,000 mg/g) indicative of nephrotic-range albuminuria because a previous study found an association between altered vitamin D metabolism and nephrotic syndrome.17,18 Finally, 4,948
subjects were included in the statistical analysis. The KNHANCES V-3 study has been conducted according to the principles expressed in the Declaration of Helsinki. (Institutional Review Board No, 2010-02CON-21-C). All participants in the survey signed an informed written consent form. Further information can be found in “The KNHANCES V-3 (2012) Sample”, which is available on the KNHANCES website. The official website of KNHANCES (http://knhanes.cdc.go.kr) is currently operating an English-language information homepage. The data of the respective year are available to everyone at the free of charge. If the applicant enters simple subscription process and his/her email address in the official website of KNHANCES, the data of the respective year can download to free of charge. If additional information is required, the readers can contact the department responsible for data (Su Yeon Park, sun4070@korea.kr).

**Results**

**Clinical characteristics of the research subjects.** The clinical characteristics of the research subjects are shown in Table 1. Serum 25(OH)D, eGFR and uACR were 20.38 ± 4.58 ng/dl, 89.78 ± 17.01 ml/min/1.73 m² and 19.30 ± 102.13 mg/g, respectively, in subjects with vitamin D deficiency (n = 3,034). The prevalence rates of decreased eGFR and elevated uACR were 3.5% (n = 107) and 8.4% (n = 254), respectively. Serum 25(OH)D, eGFR and uACR were 91.92 ± 15.15 ng/dl, 94.75 ± 19.14 ml/min/1.73 m² and 21.39 ± 130.56 mg/g, respectively, in subjects with vitamin D deficiency (n = 1,914). The prevalence rates of decreased eGFR and elevated uACR were 2.7% (n = 51) and 8.9% (n = 170), respectively.

**Clinical characteristics of the subjects according to decreased eGFR, elevated uACR and decreased GFR plus elevated uACR.** Clinical characteristics of the subjects according to decreased eGFR and elevated uACR are shown in Table 2. eGFR and uACR were 93.26 ± 16.44 ml/min/1.73 m² and 5.48 ± 5.46 mg/g for the normal group, 92.69 ± 17.60 ml/min/1.73 m² and 132.28 ± 204.03 mg/g for the elevated uACR group, 52.78 ± 6.75 ml/min/1.73 m² and 10.38 ± 7.51 mg/g for the decreased eGFR group, and 46.85 ± 12.91 ml/min/1.73 m² and 411.93 ± 726.23 mg/g for the decreased eGFR plus elevated uACR group, respectively. Variables with significant difference in normal, elevated uACR, decreased eGFR and decreased GFR plus elevated uACR group are current drink (p = 0.001), SBP (p = 0.001), DBP (p = 0.001), BMI (p = 0.001), WM (p = 0.001), TGs (p = 0.001), HDL-C (p = 0.001), BUN (p = 0.001), Crea (p = 0.001), FBG (p = 0.001) and age (p < 0.001). However, gender (p = 0.373), current smoke (p = 0.249), regular exercise (p = 0.112) and TC (p = 0.807) were not significant.

**Comparison of 25(OH)D levels and odds ratios of vitamin D deficiency according to decreased eGFR, elevated uACR and decreased GFR plus elevated uACR.** Comparison of odds ratios (ORs) of vitamin D deficiency according to decreased eGFR, elevated uACR and decreased GFR plus elevated uACR are shown in Table 3 and 4. After adjusting for the related variables (except age), the ORs of vitamin D deficiency with the normal group as a reference were significantly higher in the decreased eGFR plus elevated uACR group [3.089 (95% CI, 1.722–5.544)], but not in the elevated uACR [1.247 (95% CI, 0.986–1.577)] and decreased eGFR group [1.303 (95% CI, 0.789–2.152)]. However, when further adjusting for age, the ORs of vitamin D deficiency with the normal group as a reference were significantly higher in the elevated uACR group [1.312 (95% CI, 1.035–1.662)], decreased eGFR group [1.761 (95% CI, 1.062–2.919)] and decreased GFR plus elevated uACR group [3.549 (95% CI, 1.975–6.365)]. 25(OH)D levels (M ± SE) were 17.20 ± 0.08 ng/dl (95% CI, 17.04–17.36) for the normal group, 16.62 ± 0.30 ng/dl (95% CI, 16.04–17.21) for the elevated uACR group, 16.41 ± 0.60 ng/dl (95% CI, 15.23–17.59) for the decreased eGFR group and 13.82 ± 0.75 ng/dl (95% CI, 12.34–15.29) for the decreased GFR plus elevated uACR group (p < 0.001) (Table 4).
### Table 1. Clinical characteristics of the research subjects

| Variables              | Category             | Total (n = 4,948) | Vit. D sufficiency (n = 3,034) | Vit. D deficiency (n = 1,914) | p value |
|------------------------|----------------------|-------------------|--------------------------------|-------------------------------|---------|
| Age (year)             |                      |                   |                                |                               |         |
| ≤40                    | 1,293 (26.1)         | 642 (21.1)        | 651 (34.0)                     |                               |         |
| 40-59                  | 1,883 (38.1)         | 1,146 (37.8)      | 737 (38.5)                     |                               |         |
| ≥60                    | 1,772 (35.8)         | 1,246 (41.1)      | 526 (27.5)                     |                               |         |
| Gender                 |                      |                   |                                |                               |         |
| Men                    | 2,714 (43.9)         | 1,490 (49.1)      | 674 (35.7)                     |                               | <0.001 |
| Drinking               |                      |                   |                                |                               |         |
| Current drinker        | 2,495 (50.4)         | 1,574 (51.9)      | 921 (48.1)                     |                               | 0.005   |
| Smoking                |                      |                   |                                |                               |         |
| Current smoker         | 1,020 (20.6)         | 729 (24.0)        | 291 (15.2)                     |                               | <0.001 |
| Exercising             |                      |                   |                                |                               |         |
| Regular exerciser      | 313 (6.3)            | 218 (7.2)         | 95 (5.0)                       |                               | 0.001   |
| eGFR (ml/min/1.73 m²)  |                      |                   |                                |                               |         |
| eGFR ≥60               | 4,790 (96.8)         | 2,927 (96.5)      | 1,863 (97.3)                   |                               | 0.097   |
| eGFR <60               | 158 (3.2)            | 107 (3.5)         | 51 (2.7)                       |                               |         |
| UAM C (mg/g)           |                      |                   |                                |                               |         |
| uACR <30               | 4,524 (91.4)         | 2,780 (91.6)      | 1,744 (91.1)                   |                               | 0.529   |
| uACR ≥30               | 424 (8.6)            | 254 (8.4)         | 170 (8.9)                      |                               |         |
| BMI (kg/m²)            |                      |                   |                                |                               |         |
| ≤25                    | 23.84 ± 3.34         | 23.89 ± 3.18      | 23.76 ± 3.58                   |                               | 0.181   |
| ≥25                    | 23.22 ± 3.54         | 23.72 ± 3.26      | 23.51 ± 3.97                   |                               |         |
| SC (cm)                |                      |                   |                                |                               |         |
| ≤80                    | 81.50 ± 9.58         | 82.09 ± 9.12      | 80.57 ± 10.21                  |                               | <0.001 |
| ≥80                    | 81.20 ± 9.17         | 81.21 ± 9.21      | 81.09 ± 9.57                   |                               | 0.005   |
| SC (mmHg)              |                      |                   |                                |                               |         |
| ≤120                   | 120.08 ± 16.98       | 120.72 ± 16.70    | 119.07 ± 17.36                 |                               | 0.001   |
| ≥120                   | 120.72 ± 17.01       | 119.07 ± 17.36    | 119.07 ± 17.36                 |                               |         |
| SBP (mmHg)             |                      |                   |                                |                               |         |
| ≤90                    | 131.13 ± 87.19       | 130.88 ± 82.74    | 131.51 ± 93.12                 |                               | 0.805   |
| ≥90                    | 134.29 ± 87.19       | 131.51 ± 93.12    | 131.51 ± 93.12                 |                               |         |
| HDL-C (mg/dl)          |                      |                   |                                |                               |         |
| ≤40                    | 51.52 ± 12.63        | 51.30 ± 12.32     | 51.88 ± 12.10                  |                               | 0.113   |
| ≥40                    | 51.90 ± 12.37        | 51.88 ± 12.10     | 51.88 ± 12.10                  |                               |         |
| TBG (mg/dl)            |                      |                   |                                |                               |         |
| ≤30                    | 98.92 ± 21.78        | 99.53 ± 21.61     | 97.95 ± 22.02                  |                               | 0.013   |
| ≥30                    | 104.57 ± 22.10       | 104.57 ± 22.10    | 104.57 ± 22.10                 |                               |         |
| BUN (mg/dl)            |                      |                   |                                |                               |         |
| ≤25                    | 14.65 ± 4.99         | 15.24 ± 4.42      | 13.72 ± 4.44                   |                               | <0.001 |
| ≥25                    | 15.06 ± 5.01         | 15.06 ± 4.99      | 15.06 ± 4.99                   |                               |         |
| Crea (mg/dl)           |                      |                   |                                |                               |         |
| ≤25                    | 0.84 ± 0.23          | 0.86 ± 0.21       | 0.82 ± 0.27                    |                               | <0.001 |
| ≥25                    | 1.11 ± 0.56          | 1.11 ± 0.56       | 1.11 ± 0.56                    |                               |         |
| 25(OH)D (ng/dl)        |                      |                   |                                |                               |         |
| ≤25                    | 23.71 ± 113.79       | 22.08 ± 98.68     | 26.31 ± 134.29                 |                               | 0.203   |
| ≥25                    | 150.10 ± 84.99       | 144.78 ± 79.89    | 158.52 ± 91.89                 |                               | <0.001 |

Notes: eGFR, estimated glomerular filtration rate; uACR, urine microalbumin/creatinine ratio; BMI, body mass index; WM, waist measurement; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; HDL-C, high density lipoprotein cholesterol; FBG, fasting blood glucose; BUN, blood urea nitrogen; Crea, serum creatinine; 25(OH)D, 25-hydroxyvitamin D. Vit. D sufficiency: 25(OH)D ≥15.0 ng/dl; Vit. D deficiency: 25(OH)D <15.0 ng/dl.

### Table 2. Clinical characteristics of the subjects according to decreased eGFR, elevated uACR and decreased eGFR plus elevated uACR

| Variables      | ≤25(OH)D (ng/dl) | ≥25(OH)D (ng/dl) | Decreased eGFR (n = 93) | Decreased eGFR plus Elevated uACR (n = 65) | p value |
|----------------|-----------------|-----------------|-------------------------|---------------------------------------------|---------|
| Age (year)     |                 |                 |                         |                                             |         |
| Men            |                 |                 |                         |                                             |         |
| Current drinker|                 |                 |                         |                                             |         |
| Current smoker |                 |                 |                         |                                             |         |
| Regular exerciser |            |                 |                         |                                             |         |
| 25(OH)D (ng/dl)|                 |                 |                         |                                             |         |
| Vit. D deficiency |              |                 |                         |                                             |         |
| BMI (kg/m²)    |                 |                 |                         |                                             |         |
| SC (cm)        |                 |                 |                         |                                             |         |
| WC (cm)        |                 |                 |                         |                                             |         |
| SC (mmHg)      |                 |                 |                         |                                             |         |
| SBP (mmHg)     |                 |                 |                         |                                             |         |
| DBP (mmHg)     |                 |                 |                         |                                             |         |
| HDL-C (mg/dl)  |                 |                 |                         |                                             |         |
| FBG (mg/dl)    |                 |                 |                         |                                             |         |
| eGFR (ml/min/1.73 m²) |    |                 |                         |                                             |         |
| uACR (mg/g)    |                 |                 |                         |                                             |         |
| BUN (mg/dl)    |                 |                 |                         |                                             |         |
| Crea (mg/dl)   |                 |                 |                         |                                             |         |
| Current drinker |                 |                 |                         |                                             |         |
| Current smoker |                 |                 |                         |                                             |         |
| Regular exerciser |            |                 |                         |                                             |         |

Notes: ≤25(OH)D, 25(OH)D <60 ml/min/1.73 m² and uACR <30 mg/g; ≥25(OH)D, 25(OH)D ≥60 ml/min/1.73 m² and uACR ≥30 mg/g; Decreased eGFR, eGFR <60 ml/min/1.73 m²; Decreased eGFR plus Elevated uACR, eGFR <60 ml/min/1.73 m² and uACR ≥30 mg/g.
Discussion

In the present study, an investigation into the association between vitamin D and eGFR and uACR in Korean adults was carried out using data from the KNHANES V-3 conducted in 2012. Vitamin D deficiency was positively associated with the elevated uACR, and decreased eGFR and vitamin D level decreased greatly when decreased eGFR and elevated uACR appeared simultaneously.

Vitamin D deficiency is found in various populations worldwide in high proportions and was associated with diabetes, hypertension and insulin resistance. In particular, vitamin D deficiency patients with CKD have been associated with a higher risk of cardiovascular events and mortality and accelerate a progression of kidney disease. Ravani et al. suggested that serum 25(OH)D is an independent inverse predictor of renal disease progression and death in patients with earlier stages of CKD. However, among the research on the association between vitamin D and eGFR or uACR, previous results have been inconsistent. Park et al. reported that 25(OH)D was positively associated with eGFR ($p=0.001$) and negatively associated with uACR ($p=0.043$) in Korean adults. In contrast, O'Seaghdha et al. reported that 25(OH)D was not associated with either eGFR ($p_{\text{null}}=0.3$) or uACR ($p_{\text{null}}=0.9$) in the Framingham Heart Study. In the present study, after adjusting for the related variables (except age), the association between vitamin D and elevated uACR and decreased eGFR group was not significant, and these results were similar to the study of O'Seaghdha et al. However, when further adjusting for age, the ORs of vitamin D deficiency with the normal group as a reference were significantly higher in the elevated uACR group [1.312 (95% CI, 1.035–1.662)] and decreased eGFR group [1.761 (95% CI, 1.062–2.919)], and these results were similar to the study of Park et al. Age is a strong risk factor of albuminuria and CKD. In our results, the prevalence of elevated uACR and decreased eGFR levels were increased as an increase of age, but the prevalence of vitamin D deficiency was decreased (Fig. 1). Vitamin D was increased as an increase of the age because the outdoor activity in the Korean elderly is higher than in the younger. However, aging affects the formation of 1,25(OH)$_2$D, the active form of vitamin D. Although vitamin D [25(OH)D] increases, production of 1,25(OH)$_2$D is reduced by 50% as a result of a decline in renal function according to increase of age. Therefore, some studies emphasized that need to measure both 25(OH)D and 1,25(OH)$_2$D in vitamin D deficiency.

We examined the ORs of vitamin D deficiency when the decreased eGFR and elevated uACR occurred simultaneously. It is important to monitor uACR levels in populations with CKD. Albuminuria is an unequivocal surrogate marker for CKD progression as well as future cardiovascular events and its reduction is used as a treatment goal for these diseases. In addition, albuminuria is an early warning sign of diabetic nephropathy (DN), and DN is associated with an elevated risk of progression toward ESRD as well as increase of cardiovascular events and mortality. In the present study, the ORs of vitamin D deficiency in the decreased eGFR plus elevated uACR group [3.549 (95% CI, 1.975–6.365)] was very higher than the elevated uACR group [1.312 (95% CI, 1.035–1.662)] or decreased eGFR group [1.761 (95% CI, 1.062–2.919)]. We thought these results that the synergistic interaction between the decreased eGFR and elevated uACR. Levey et al. suggested that the synergistic interaction between the decreased eGFR and elevated uACR. They reported that the progressive CKD in the decreased eGFR plus elevated uACR group (at least 9.4 times, up to 57 times) was greatly higher than the elevated uACR group (at least 0.4 times, up to 8.1 times). In particular, the OR of end stage renal disease (ESRD) for the decreased eGFR plus elevated uACR group (at least 9.4 times, up to 57 times) was very higher than the elevated uACR group (at least 0.4 times, up to 8.1 times). Vitamin D from the diet or skin synthesis is biologically inactive and is converted to 25(OH)D in the liver. And then,

Table 3. Comparisons of vitamin D deficiency odds ratios according to decreased eGFR, elevated uACR and decreased eGFR plus elevated uACR

| Variables | Category | Model 1 | Model 2 | Model 3 | Model 4 |
|-----------|----------|---------|---------|---------|---------|
| Normal    | eGFR ≥60 and uACR <30 | 1       | 1       | 1       | 1       |
| Elevated uACR | uACR ≥30 | 1.070 (0.859–1.332) | 1.208 (0.961–1.517) | 1.247 (0.986–1.577) | 1.312 (1.035–1.662) |
| Decreased eGFR | eGFR <60 | 0.613 (0.388–0.968) | 0.709 (0.445–1.127) | 1.303 (0.789–2.152) | 1.761 (1.062–2.919) |
| Decreased eGFR plus Elevated uACR | eGFR <60 and uACR ≥30 | 0.987 (0.597–1.633) | 1.172 (0.702–1.959) | 3.089 (1.722–5.544) | 3.549 (1.975–6.365) |

25(OH)D, 25-hydroxyvitamin D; eGFR, estimated glomerular filtration rate; uACR, urine microalbumin/creatinine ratio. Model 1 (odds ratio (OR), 95% CI), Non-adjusted; Model 2 (OR, 95% CI), adjusted for alcohol drinking, SBP, DBP, BMI and WM; Model 3 (OR, 95% CI), Model 2 further adjusted for TGs, HDL-C, BUN and FBG; Model 4 (OR, 95% CI), Model 3 further adjusted for age.

Table 4. Comparisons of 25(OH)D levels according to decreased eGFR, elevated uACR and decreased eGFR plus elevated uACR

| Variables | Category | 25(OH)D levels (ng/dl) |
|-----------|----------|-----------------------|
| Normal    | eGFR ≥60 and uACR <30 | 17.11 ± 0.08 (16.95–17.28) |
| Elevated uACR | uACR ≥30 | 16.78 ± 0.30 (16.19–17.37) |
| Decreased eGFR | eGFR <60 | 18.58 ± 0.58 (17.44–19.72) |
| Decreased eGFR plus Elevated uACR | eGFR <60 and uACR ≥30 | 16.55 ± 0.70 (15.18–17.91) |

p value: 0.039, 0.001, <0.001

25(OH)D, 25-hydroxyvitamin D; eGFR, estimated glomerular filtration rate; uACR, urine microalbumin/creatinine ratio. Model 1 (Mean ± SE, 95% CI), alcohol drinking, SBP, DBP, BMI and WM; Model 2 (Mean ± SE, 95% CI), Model 1 further adjusted for TGs, HDL-C, BUN and FBG; Model 3 (Mean ± SE, 95% CI), Model 2 further adjusted for age.
25(OH)D is further hydroxylated in the kidneys to form 1,25(OH)\(_2\)D which is the biologically active form of vitamin D.\(^{(36)}\) However, in patients with CKD, there is high rate of prevalence of vitamin D deficiency because the reduced ability to convert the active form 1,25(OH)\(_2\)D.\(^{(37)}\) Therefore, if renal function decreases rapidly by the synergistic interaction between the decreased eGFR and elevated uACR, the frequency of vitamin D deficiency may increase. On the other hand, renal function may decrease as vitamin D deficiency. Vitamin D is known to suppress the renin gene transcription,\(^{(38)}\) and administration of vitamin D preparations such as calcitriol and paricalcitol inhibit renin expression and consequently reduce angiotensin II expression.\(^{(39)}\) Angiotensin II is a key mediator of proteinuria, raises efferent glomerular arteriole resistance and induces transforming growth factor (TGF)-\(\beta\)\(_1\), which inhibits cell proliferation and increases apoptosis in the kidney,\(^{(40,41)}\) and so the reduction of angiotensin II by vitamin D may be a mechanism to counter these effects. NF-\(\kappa\)B is involved in the regulation of inflammatory cytokines that may promote inflammation and fibrogenesis in kidney disease.\(^{(42)}\) In mice with obstructive nephropathy, administration of paricalcitol was found to block NF-\(\kappa\)B and attenuate tubule-interstitial inflammation.\(^{(43)}\) Cohen-Lahav et al.\(^{(44)}\) reported that vitamin D upregulates IkappaBalpaha (I\(\kappa\)B\(\alpha\)) levels by increasing mRNA stability; an increase in I\(\kappa\)B\(\alpha\) levels reduces nuclear translocation of NF-\(\kappa\)B and thereby downgrades its activity. It is unclear whether the decrease of renal function increased the incidence of vitamin D deficiency, or vitamin D deficiency decreases the renal function. Furthermore, the association between the decrease of renal function and vitamin D is still debated. In the relationship between vitamin D and CKD and albuminuria, the result may differ according to the country and ethnicity, study population and the use of different reference GFR methods. In Asian, MDRD and CKD-EPI Equations for Taiwanese and Japanese adults is modified for their studied population. However, there is no definite modified model for Korean adults yet. Therefore, research is necessary to modify the MDRD and CKD-EPI Equations for the Korean adults.

There are a few limitations in the present study. First, season is the most important determinant of serum 25(OH)D levels, but the data of the KNHANES V-3 study did not specify serum 25(OH)D levels according to season. Second, serum calcium concentration and daily intake of vitamin D are important determinants of serum 25(OH)D levels, but these were not measured as part of the KNHANES V-3 study. Therefore, serum calcium concentration and daily intake volume of vitamin D could not be used as an adjustment variable. Third, parathyroid hormone (PTH) is an important determinant of serum vitamin D levels as increased PTH promotes calcium influx into adipocytes, where intracellular calcium enhances lipogenesis.\(^{(45)}\) Therefore, serum vitamin D levels could change depending on serum PTH. However, in the data from the KNHANES V-3 study, there are no measurements of PTH of the participants (adults \(\geq 20\) years of age). The serum 25(OH)D levels for each season, along with calcium and PTH levels, should be included as variables of vitamin D status in future studies. Fourth, because this was a cross-sectional study, the ability to establish a causal relationship between vitamin D and uACR and eGFR was limited. Therefore, more accurate results might be obtained by performing a cohort study by adding these variables.

**Conclusion**

The present study investigated the association between serum 25(OH)D and urine microalbumin/creatinine ratio and estimated glomerular filtration rate in Korean adults using data from the KNHANES V-3 conducted in 2012. Vitamin D deficiency was positively associated with the elevated uACR and decreased eGFR. In addition, vitamin D level decreased greatly when decreased eGFR and elevated uACR appeared simultaneously.

**Conflict of Interest**

We have not received any financial support or other benefits from commercial sources for the work reported in the manuscript. None of the authors have financial interests that could create a potential conflict of interest or appearance of a conflict of interest with regard to this work.
References

1. Muntner P, He J, Hamm L, Loria C, Whelton PK. Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. J Am Soc Nephrol 2012; 13: 745–753.

2. Coresh J, Astor BC, Greene T, Eknayan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003; 41: 1–12.

3. U.S. Renal Data System. Annual Data Report: Atlas of End-Stage Renal Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland. 2003.

4. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39: S1–S266.

5. De Leeuw PW, Thijs L, Birkenhager WH, et al. Prognostic significance of renal function in elderly patients with isolated systolic hypertension: results from the Syst-Eur trial. J Am Soc Nephrol 2002; 13: 2213–2222.

6. Huniscker LG, Adler S, Caggida A, et al. Predictors of the progression of renal disease in the Modification of Diet in Renal Disease Study. Kidney Int 1997; 51: 1908–1919.

7. Viberni GC, Wiseman MJ. The kidney in diabetes: significance of the early abnormalities. Clin Endocrinol Metab 1986; 15: 753–782.

8. Aguado P, del Campo MT, Garcia MV, et al. Low vitamin D levels in outpatient postmenopausal women from a rheumatology clinic in Madrid, Spain: their relationship with bone mineral density. Osteoporos Int 2000; 11: 739–744.

9. Levin A, Bakris GL, Molitch M, et al. Hypertension and increased left ventricular mass in African-American patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney Int 2007; 71: 31–38.

10. Hollis BW, Horst RL. The assessment of circulating 25(OH)D and 1,25(OH)₂D: where we are and where we are going. J Steroid Biochem Mol Biol 2010; 113: 473–476.

11. Choi HS, Kim KA, Lim CY, et al. Low serum vitamin D is associated with high risk of diabetes in Korean adults. J Nutr 2011; 141: 1524–1528.

12. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357: 266–281.

13. Melamed ML, Thadhani RI. Vitamin D therapy in chronic kidney disease. Kidney Int 2007; 71: 358–365.

14. Gal-Moscovici A, Sprague SM. Use of vitamin D in chronic kidney disease patients. Kidney Int 2010; 78: 146–151.

15. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis 2014; 63: 713–735.

16. Jung IK. Prevalence of vitamin D deficiency in Korea: results from KNHANES 2010 to 2011. J Nutr Health 2013; 46: 540–551.

17. Saha H. Calcium and vitamin D homeostasis in patients with chronic kidney disease: a systematic review. Osteoporos Int 1994; 4: 290–296.

18. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150: 604–612.

19. Yoon H, Kim GS, Kim SG, Moon AE. The relationship between metabolic syndrome and increase of metabolic syndrome score and serum vitamin D levels in Korean adults: 2012 Korean National Health and Nutrition Examination Survey. Clin Endocrinol Metab 2015; 57: 82–87.

20. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and metaanalysis. J Clin Endocrinol Metab 2007; 92: 2017–2029.

21. Danik JS, Manson JE. Vitamin D and cardiovascular disease. Circulation Cardiovasc Med 2012; 14: 414–424.

22. Wang TJ, Pencina MJ, Booth SL, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation 2008; 117: 503–511.

23. Ravan P, Malberti F, Tripepi G, et al. Vitamin D levels and patient outcome in chronic kidney disease. Kidney Int 2009; 75: 88–95.

24. Park J, Ryu SY, Han MA, Choi SW. The association of vitamin D with estimated glomerular filtration rate and albuminuria: 5th Korean National Health and Nutritional Examination Survey 2011–2012. J Ren Nutr 2016; 26: 360–366.

25. O’Seaghdha CM, Hwang SJ, Holden R, Booth SL, Fox CS. Phylloquinone and vitamin D status: associations with incident chronic kidney disease in the Framingham Offspring cohort. Am J Kidney Dis 2012; 59: 68–77.

26. Kang YU, Bae EH, Ma SK, Kim SW. Determinants and burden of chronic kidney disease in a high-risk population in Korea: results from a cross-sectional study. Korean J Intern Med 2016; 31: 920–929.

27. Chwota NK, Pant P, Chwota MN. Microalbuminuria in diabetes mellitus: association with age, sex, weight, and creatinine clearance. Indian J Nephrol 2009; 19: 53–56.

28. Choi HS, Oh HJ, Choi H, et al. Vitamin D insufficiency in Korea—a greater threat to younger generation: the Korea National Health and Nutrition Examination Survey (KNHANES) 2008. J Clin Endocrinol Metab 2011; 96: 643–651.

29. Gallagher JC. Vitamin D and aging. Endocrinol Metab Clin North Am 2013; 42: 319–332.

30. Lips P. Relative value of 25(OH)D and 1,25(OH)₂D measurements. J Bone Miner Res 2002; 22: 1668–1671.

31. Lagunova Z, Porojnicu AC, Vieth R, Lindberg FA, Hesseberg S, Moan J. Serum 25-hydroxyvitamin D is a predictor of serum 1,25-dihydroxyvitamin D in overweight and obese patients. J Nutr 2011; 141: 112–117.

32. de Zeeuw D, Remuzzi G, Parving HH, et al. Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. Circulation 2004; 110: 921–927.

33. Gerstein HC, Mann JF, Pogue J, et al. Prevalence and determinants of microalbuminuria in high-risk diabetic and nondiabetic patients in the Heart Outcomes Prevention Evaluation Study. The HOPE Study Investigators. Diabetes Care 2000; 23 Suppl 2: B35–B39.

34. Van Dijk PC, Kager JK, Stengel B, Grönhagen-Riska C, Feest TG, Briggs JD. Renal replacement therapy for diabetic end-stage renal disease: data from 10 registries in Europe (1991–2000). Kidney Int 2005; 67: 1489–1499.

35. Sarafidis PA, Bakris GL. Microalbuminuria and chronic kidney disease as risk factors for cardiovascular disease. Nephrol Dial Transplant 2006; 21: 2366–2374.

36. Holick MF, Schnoes HK, DeLuca HF, Suda T, Cousins RJ. Analogos of 1,25-dihydroxycholecalciferol. A metabolite of vitamin D active in intestine. Biochemistry 1971; 10: 2799–2804.

37. Williams S, Malatesta N, Norris K. Vitamin D and chronic kidney disease. Ethn Dis 2009; 19 (4 Suppl 5): S5–S11.

38. Li YC, Qiao G, Uskokovic M, Zheng W, Kong J. Vitamin D: a negative endocrine regulator of the renin-angiotensin system and blood pressure. J Steroid Biochem Mol Biol 2004; 89–90 (1–5): 387–392.

39. Qiao G, Kong J, Uskokovic M, Li YC. Analogos of 1alpha,25-dihydroxyvitamin D(3) as novel inhibitors of renin biosynthesis. J Steroid Biochem Mol Biol 2005; 96: 59–66.

40. Ruster C, Wolf G. Renin-angiotensinaldosterone system and progression of renal disease. J Am Soc Nephrol 2006; 17: 2985–2991.

41. Kobori H, Nakagaku M, Nahirneyama A. The intrarenal renin-angiotensin system: from physiology to the pathobiology of hypertension and kidney disease. Pharmacol Rev 2007; 59: 251–287.

42. Gujarro C, Egido J. Transcription factor κB (NF-κB) and renal disease. Kidney Int 2001; 59: 415–424.

43. Tan X, Li Y, Liu Y. Paricalcitol attenuates renal interstitial fibrosis in obstructive nephropathy. J Am Soc Nephrol 2006; 17: 3382–3393.

44. Cohen-Lavhat M, Shany S, Tohvin D, Chaimovicz C, Doudevani A. Vitamin D decreases NFκB activity by increasing IkBα levels. Nephrol Dial Transplant 2006; 21: 889–897.

45. Snijder MB, van Dam RM, Visser M, et al. Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. J Clin Endocrinol Metab 2005; 90: 4119–4123.