The Prevalence of 25-hydroxyvitamin D Deficiency in Japanese Patients with Diabetic Nephropathy

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Abstract

Objective The purpose of this study was to measure serum 25-hydroxyvitamin D [25(OH)D] levels in Japanese patients with diabetic nephropathy and determine the relationship between 25(OH)D concentrations and various factors.

Methods The study subjects included 442 patients with type 2 diabetes. Their serum levels of creatinine, HbA1c, intact-parathyroid hormone, urinary albumin, 25(OH)D, and 1,25-dihydroxyvitamin D [1,25(OH)2D] were measured and their estimated glomerular filtration rate (eGFR) was determined. The patients were divided into four groups based on the risk for progression to chronic kidney disease (CKD): low, moderate, high, very high, based on their eGFR and their level of albuminuria.

Results The median 25(OH)D level was 14.6 ng/mL; 11% of the patients had 25(OH)D deficiency (<10 ng/mL), and 2% of patients had active vitamin D deficiency, as defined by a 1,25(OH)2D level of <22 pg/mL. The serum 25(OH)D level was correlated with the serum 1,25(OH)2D level in patients with a very high risk for CKD, but not in those with a moderate or high risk for CKD.

Conclusion Although the vitamin D levels of the Japanese patients with diabetic nephropathy and CKD were low, the prevalence of vitamin D deficiency, as defined by the 1,25(OH)2D level, was low. Albuminuria, younger age, and female gender were associated with a low 25(OH)D level. The serum level of 25(OH)D should be monitored to assess the vitamin D status of patients with nephropathy and CKD.

Key words: vitamin D, diabetic nephropathy, chronic kidney disease

The low levels of active vitamin D that occur in the kidneys, where 25(OH)D is converted to 1,25(OH)2D, is considered to be diagnostic of vitamin D deficiency. The second hydroxylation step occurs in the liver. Low levels of active vitamin D might be caused by the reduced reuptake of 25(OH)D in tubular cells under proteinuric conditions (7, 8).

There is little or no information on the 25(OH)D levels in Japanese patients with CKD. This is probably due to the fact that the Japanese Government-based health insurance does not cover the costs of these measurements and/or treatments (18). In this study, the serum 25(OH)D levels of Japanese patients with diabetic nephropathy were measured and the relationships between the 25(OH)D concentrations and other factors were investigated.

Materials and Methods

The study subjects included 442 patients with nephropathy associated with type 2 diabetes mellitus. They represented all such patients who were treated at the outpatient clinic at Tokai University Hospital between February and April 2013, after the exclusion of patients on dialysis. In accordance with the Japan modified Kidney Disease Improving Global Outcomes (KDIGO) guidelines, the patients’ levels of albuminuria were classified as stages A1 to A3, while their glomerular filtration rates were classified as stages G1 to G5 (19) (Table 1). Ethical approval for this study was granted by the Tokai University Institution Review Board for Clinical Research, and all participants provided written informed consent.

Blood and urine samples, and clinical data were simultaneously collected between February and April 2013. The serum levels of creatinine, HbA1c (National Glycohemoglobin Standardization Program), intact parathyroid hormone (iPTH), urinary albumin, estimated glomerular filtration rate (eGFR), 25(OH)D, and 1,25(OH)2D were measured. The level of 25(OH)D was measured using a chemiluminescent immunnoassay (Abbott Laboratories, Chicago, USA), the level of 1,25(OH)2D was measured by a radioimmunoassay (Diasorin, Saluggia, Italy), and iPTH was determined using an electro-chemiluminescence immunoassay (Roche Diagnostics, Basel, Switzerland). The corrected calcium and phosphorus levels, and the proteinuria, and alkaline phosphatase (ALP) levels were measured using standard methods.

Vitamin D deficiency was defined as a 25(OH)D level of <10 ng/mL; insufficiency was defined as a 25(OH)D level of <20 ng/mL (20, 21). Values ≥20 ng/mL were considered normal. 1,25(OH)2D levels of <22 pg/mL were considered to reflect active vitamin D deficiency (9). Hyperparathyroidism was defined as an iPTH level of >65 ng/mL (9).

All numerical data were expressed as the mean ± standard deviation (SD) or median (interquartile range). Differences among groups, based on the risk of progression to CKD and the 25(OH)D level, were tested with the Kruskal-Wallis test followed by the Dunn test. The prevalence of deficiency was compared using the chi-squared test with a 2-way contingency table. A logistic regression analysis was also used to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) for patients with low 25(OH)D levels. The exponential transformation of variables was performed as needed to improve their normality. The correlation between the 25(OH)D and 1,25(OH)2D levels was evaluated using Pearson’s test and Passing-Bablok fit was used for the linear regression analysis. Statistical analyses were performed using the JMP (version 10.0.0, SAS Institute, Cary, USA) and Analyse-it (version 3.53, Analyse-it Software, Leeds, UK) software programs.

### Table 1. Distribution of eGFR and Albuminuria (n=442).

<table>
<thead>
<tr>
<th>eGFR (mL/min)</th>
<th>Albuminuria (mg/g Cr)</th>
<th>A1 (≤30)</th>
<th>A2 (30-299)</th>
<th>A3 (≥ 300)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 (&lt; 90)</td>
<td>35 (7.9)</td>
<td>12 (2.7)</td>
<td>3 (0.7)</td>
<td>50 (11)</td>
<td></td>
</tr>
<tr>
<td>G2 (90-89)</td>
<td>116 (26.2)</td>
<td>51 (11.5)</td>
<td>31 (7.0)</td>
<td>198 (45)</td>
<td></td>
</tr>
<tr>
<td>G3a (45-59)</td>
<td>30 (8.8)</td>
<td>28 (6.3)</td>
<td>29 (6.6)</td>
<td>66 (22)</td>
<td></td>
</tr>
<tr>
<td>G3b (30-44)</td>
<td>16 (3.6)</td>
<td>20 (4.5)</td>
<td>26 (5.9)</td>
<td>62 (14)</td>
<td></td>
</tr>
<tr>
<td>G4 (15-29)</td>
<td>1 (0.2)</td>
<td>9 (2.0)</td>
<td>16 (3.6)</td>
<td>26 (5.9)</td>
<td></td>
</tr>
<tr>
<td>G5 (&lt; 15)</td>
<td>0 (0.0)</td>
<td>1 (0.2)</td>
<td>9 (2.0)</td>
<td>10 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>207 (47)</td>
<td>121 (27)</td>
<td>114 (26)</td>
<td>442 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Data are number and (percentage) of patients.

Ranking of progression risk of CKD was classified by eGFR and albuminuria, 2012 classification (15). The low-risk group included patients classified as G1 or G2 (eGFR >60 mL/min/1.73 m2) with A1 (urinary albumin <30 mg/g.Cr). The moderate risk group; light gray, included patients classified as G3a (45-59) with A1, and G1 or G2 with A2 (30-299). The high risk group; gray, included patients classified as G3b (30-44) with A1, A3 with A2, or G1 or G2 with A3 (>300). The very high risk group included patients classified as G4-G5 (<30) with A1 (<30), G3b-G5 (<45) with A2 or G3a-G5 (<60) with A3.

One third of patients were classified as low risk, 23% as moderately increased risk, 18% as high risk, and 25% as very high risk of progression of CKD.
Table 2. Patient Characteristics by Risk of Progression of Chronic Kidney Disease (CKD).

<table>
<thead>
<tr>
<th>Ranking of progression risk of CKD (2012 classification)</th>
<th>Low risk (n=151)</th>
<th>Moderate risk (n=102)</th>
<th>High risk (n=78)</th>
<th>Very high risk (n=111)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.3±13.1</td>
<td>66.6±11.6</td>
<td>67.8±11.1</td>
<td>68.4±12.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>71.5</td>
<td>76.2</td>
<td>67.2</td>
<td>68.9</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.9±4.7</td>
<td>25.6±5.2</td>
<td>26.1±4.4</td>
<td>25.4±4.4</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.2±0.3</td>
<td>4.2±0.3</td>
<td>4.0±0.3</td>
<td>3.8±0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ca (mg/dL)</td>
<td>9.5±0.4</td>
<td>9.3±0.4</td>
<td>9.4±0.4</td>
<td>9.4±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>P (mg/dL)</td>
<td>3.2±0.5</td>
<td>3.2±0.5</td>
<td>3.2±0.5</td>
<td>3.5±0.7</td>
<td>0.0004</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>216 (187-274)</td>
<td>230 (191-269)</td>
<td>251 (202-325)</td>
<td>252 (213-312)</td>
<td>0.01</td>
</tr>
<tr>
<td>iPTH (pg/mL)</td>
<td>40 (33-50)</td>
<td>41 (32-52)</td>
<td>46 (35-64)</td>
<td>64 (46-97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>25(OH)D (ng/mL)</td>
<td>14.3 (11.8-18.2)</td>
<td>16.4 (12.5-19.9)</td>
<td>13.4 (11.2-18.1)</td>
<td>14.3 (11.6-18.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>1,25(OH)2D (pg/mL)</td>
<td>57 (47-70)</td>
<td>54 (46-64)</td>
<td>46 (37-55)</td>
<td>43 (34-54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>7.1±1.2</td>
<td>7.2±1.2</td>
<td>7.2±1.1</td>
<td>6.9±1.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean±SD (Age BMI, Albumin, Ca, P and HbA1C), median values and interquartile range (ALP, iPTH, 25(OH)D and 1,25(OH)2D), or percentages (males).

Ranking of progression risk of CKD was classified by eGFR and albuminuria, 2012 classification (19). p values represent differences among the four risk groups, by Kruskal-Wallis test and Pearson chi-square test (male).

BMI: body mass index, ALP: alkaline phosphatase, iPTH: intact parathyroid hormone, Ca: corrected calcium, P: phosphorus, 25(OH)D: 25-hydroxyvitamin D, 1,25(OH)2D: 1,25-dihydroxyvitamin D.

Results

The study population consisted of 290 men (mean age, 66 years; range, 22-89 years) and 152 women (mean age, 64 years; range, 24-91 years). At study entry, the patients were classified according to their risk of progression to CKD, using their albuminuria level and eGFR, according to the Japan-modified KDIGO guidelines (19) (Table 1). The eGFR was classified as stage G2 in 198 patients while albuminuria was classified as stage A1 in 207 patients. An analysis of risk of progression to CKD showed that 151 patients (34%) had a low risk of progression (G1 or G2 with A1), 102 (23%) had a moderate risk of progression (G3a with A1, and G1 or G2 with A2), 78 (18%) had a high risk of progression (G3b with A1, G3a with A2, and G1 or G2 with A3) and 111 (25%) had a very high risk of progression (others).

The plotting of the 25(OH)D and 1,25(OH)2D data of all of the patients showed skewed distribution patterns. The mean, median and maximum 25(OH)D levels in all patients were 15.6, 14.6, and 35.4 ng/mL, respectively; 70% of the patients showed an insufficient (10-20 ng/mL) 25(OH)D level, and 11% of the patients showed a deficient 25(OH)D level (<10 ng/mL). On the other hand, only 2% of patients showed a deficient 1,25(OH)2D level (<22 ng/mL). The mean, median and maximum 1,25(OH)2D levels were 52.7, 51.1, and 98.4 pg/mL, respectively.

Table 2 summarizes the clinical backgrounds of the patients and the differences between the groups stratified by the risk of progression to CKD. The patients in the high and very high risk groups were significantly older. The serum phosphorus levels of the patients in the very high risk group were significantly higher than those in the other groups (p=0.0004), but calcium levels did not differ to a statistically significant extent. There were significant differences in the serum albumin, ALP, iPTH, and 1,25(OH)2D levels of the risk groups. The ALP and iPTH levels increased as the level of risk increased, whereas the 1,25(OH)2D and serum albumin levels decreased as the level of risk increased. There were no significant differences in the gender, body mass index (BMI), or HbA1C level of the patients in the different risk groups.

Fig. 1 shows the median 25(OH)D, 1,25(OH)2D, and iPTH values according to the eGFR levels. There were no significant differences in 25(OH)D, 1,25(OH)2D, and iPTH levels as the eGFR decreased from >90 to 60 mL/min. However, as the eGFR continued to decrease to <15 mL/min, there was a statistically significant increase in the iPTH levels and a decrease in 1,25(OH)2D level (Fig. 1B and C).

An analysis of the data after the classification of the patients' eGFRs into G grades showed a significant difference in the 1,25(OH)2D levels of the G2 and G3a groups, and significant difference in the iPTH levels of the G3a and G3b groups. There was no significant change in the 25(OH)D level with the deterioration of the eGFR (Fig. 1).

The prevalence of 25(OH)D deficiency (<10 ng/mL), 1,25(OH)2D deficiency (<22 pg/mL), and hyperparathyroidism (iPTH >65 pg/mL), stratified according to the eGFR, is shown in Fig. 2. Patients with a low eGFR (<15 mL/min/1.73 m²; n=10) had low 25(OH)D and 1,25(OH)2D levels and high iPTH levels. There were increasing trends in the all prevalences among the eGFR groups, and these differences reach statistical significance on 1,25(OH)2D deficiency and hyperparathyroidism [p<0.05 (chi-squared test)]. However, there were no significant differences on the prevalences of 25(OH)D deficiency. In general, 1,25(OH)2D deficiency was not noted in patients with an eGFR of ≥15 mL/min/1.73 m².

Table 3 shows the characteristics of patients categorized according to their serum 25(OH)D levels. There were significant differences (p<0.05) in age, gender, serum cre-
A. Serum 25(OH)D

B. Serum 1,25(OH)₂D

C. Serum iPTH

Figure 1. The median values (interquartile range) of serum 25(OH)D, 1,25(OH)₂D, and iPTH stratified by the eGFR. A: serum 25(OH)D, B: serum 1,25(OH)₂D, C: serum iPTH. *p<0.05 vs. 1,25(OH)₂D, **p<0.05 vs. iPTH (Dunn test). 25(OH)D: serum 25-hydroxyvitamin D, 1,25(OH)₂D: 25-dihydroxyvitamin D, iPTH: intact parathyroid hormone, eGFR: estimated glomerular filtration rate

Figure 2. The prevalence of 25(OH)D deficiency, 1,25(OH)₂D deficiency, and hyperparathyroidism, stratified by the eGFR. See Figure 1 for the definitions of the abbreviations.
Table 3.  Patient Characteristics according to Serum 25(OH)D Level.

<table>
<thead>
<tr>
<th>25(OH)D level (ng/mL)</th>
<th>Deficiency (&lt;10) (n=47)</th>
<th>Insufficiency (10-20) (n=311)</th>
<th>Normal (&gt;20) (n=84)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.2±15.7</td>
<td>64.5±12.8</td>
<td>70.6±7.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Males (%)</td>
<td>38.3</td>
<td>64.0</td>
<td>86.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.4±7.4</td>
<td>25.4±4.4</td>
<td>24.7±3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.9±0.6</td>
<td>4.1±0.4</td>
<td>4.1±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.35±1.25</td>
<td>0.99±0.6</td>
<td>1.07±0.4</td>
<td>0.003</td>
</tr>
<tr>
<td>eGFR (min/mL)</td>
<td>58±29</td>
<td>65±24</td>
<td>58±17</td>
<td>0.04</td>
</tr>
<tr>
<td>Ca (mg/dL)</td>
<td>9.4±0.5</td>
<td>9.4±0.4</td>
<td>9.4±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>P (mg/dL)</td>
<td>3.4±0.7</td>
<td>3.3±0.5</td>
<td>3.2±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>244 (209-313)</td>
<td>228 (193-290)</td>
<td>229 (194-291)</td>
<td>NS</td>
</tr>
<tr>
<td>iPTH (pg/mL)</td>
<td>63 (44-104)</td>
<td>45 (35-60)</td>
<td>40 (35-58)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1,25(OH)₂D (pg/mL)</td>
<td>47 (37-56)</td>
<td>52 (43-63)</td>
<td>55 (44-67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.2±1.3</td>
<td>7.1±1.2</td>
<td>6.9±1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Proteinuria (g/g.Cr)</td>
<td>0.23 (0.08-1.72)</td>
<td>0.13 (0.07-0.52)</td>
<td>0.12 (0.05-0.39)</td>
<td>0.049</td>
</tr>
<tr>
<td>Albuminuria (mg/g.Cr)</td>
<td>80 (19-1,300)</td>
<td>35 (14-309)</td>
<td>23 (12-211)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Data are mean±SD (age, BMI, albumin, serum creatinine, eGFR, Ca, P, and HbA1c), median and interquartile range (ALP, intact PTH, 1,25(OH)₂D, proteinuria and albuminuria), or percentage (males).

Differences in 25(OH)D levels were tested by the Kruskal-Wallis test.
Differences in percentages of males were tested by Pearson chi-square test.
See Table 2 for abbreviations.

Figure 3.  The factors associated with a low 25(OH)D level (15 ng/mL) in a multivariate regression analysis. The relative quality of the statistical model: AIC=474.13 BIC=521.06

The present study showed a significant correlation between the serum 1,25(OH)₂D level (but not the 25(OH)D level) and the risk of CKD progression in Japanese patients. Furthermore, the serum albumin, iPTH, and ALP levels (but not gender, BMI, or HbA1c) were significantly correlated with the risk of CKD progression. These findings are in agreement with those of a previous US study that showed a close relationship between the eGFR and the 1,25(OH)₂D level, but not the 25(OH)D level (9).

Finally, the serum 1,25(OH)₂D and 25(OH)D levels were compared according to the relative risk of progression (Fig. 4). In the low-risk and very high risk groups (Fig. 4B and E), the 25(OH)D level was correlated with the 1,25(OH)₂D (r=0.31 and r=0.44 respectively). This correlation was not observed in the moderate or high risk groups (Fig. 4C and D). Furthermore, a linear regressions analysis using the Passing-Bablok fit showed that the data slopes of the low-risk and very high risk groups were similar.

Discussion

The correlation between the 25(OH)D levels and various clinical parameters was also examined. The 25(OH)D level was significantly correlated with age, serum creatinine, 1,25(OH)₂D, and iPTH, but weakly correlated with HbA1c, eGFR, proteinuria, and albuminuria.

A logistic regression analysis that included the factors associated with low 25(OH)D levels was performed using a cutoff value of 15 ng/mL, which represented the midpoint between deficiency (10 ng/mL) and insufficiency (20 ng/mL). Among age, gender, BMI, eGFR, corrected Ca, P, ALP, PTH, HbA1c, micro-albuminuria (30-300 mg/g.Cr) and macro-albuminuria (>300 mg/g.Cr), identified macro-albuminuria (OR, 2.17; 95%CI, 1.13-4.23) and female gender (OR, 3.85; 95%CI: 2.27-7.14) were associated with low 25(OH)D levels (Fig. 3).

In the present study, 11% of the patients were 25(OH)D deficient (<10 ng/mL); however, a large number of patients (34%) showed a low risk for CKD progression. The prevalence of 25(OH)D deficiency in patients with CKD stages 4 and 5 was higher than that in patients with CKD stages 1-3 (28% vs. 9%, respectively). This was most likely due to the presence of diabetic nephropathy and high albuminuria (10-12).
A decline in 25(OH)D reuptake in the proximal renal tubules is one possible mechanism of vitamin D deficiency in patients with CKD, especially those with diabetic nephropathy (10). 25(OH)D that is filtered by the glomeruli can be released into the urine by a reduction in the reuptake in the proximal tubules, because this process is mediated by megalin and can result in the release of 25(OH)D as well as protein reuptake (5, 8). Vitamin D deficiency is therefore associated with an increased risk of albuminuria. In the present study, albuminuria was associated with a decreased 25(OH)D level, and our results support the findings of a previous study (22).

Vitamin D deficiency is known to occur in patients with kidney disease. In comparison to previous studies (9-11, 20, 23, 24), a higher percentage of patients in our study exhibited 25(OH)D deficiency. The 25(OH)D concentration was <15 ng/mL in more than half of the Japanese patients in this study. In contrast, the concentration was <15 ng/mL in only 10-40% of the CKD patients in previous studies (9, 23-26). One possible reason for this difference could be racial differences among the patient groups, since the main source of vitamin D is synthesis from the skin by sunlight, which differs among the races (2, 27, 28). Another reason could be the study period; the patients were enrolled in the winter season when 25(OH)D levels are usually lower due to shorter periods of sunlight (20, 29). In comparison, the patients of previous studies were enrolled in the summer season or throughout the year (9-11, 20, 23, 24).

It is noteworthy that only 2% of patients in the present study showed active vitamin D deficiency as defined by 1,25(OH)2D levels of <22 pg/mL, and most patients in the early stages of CKD had normal iPTH levels. These findings suggest the need to establish an alternative threshold for 25(OH)D insufficiency for Japanese patients.

Based on the KDIGO guidelines (15), simple vitamin D supplementation is recommended for patients with low vitamin D levels. Several studies have reported the benefits of vitamin D therapy in patients with diabetic nephropathy (8, 30). Treatment with cholecalciferol was reported to effectively increase both serum 25(OH)D and 1,25(OH)2D in patients with type 2 diabetes and CKD (31). These increases were accompanied by decreases in the urine albumin-to-creatinine ratio and transforming growth factor-β1 levels (32). Our results suggest that 1,25(OH)2D levels may correlate with 25(OH)D levels with progressive albuminuria, and that intervention may be clinically reasonable in patients who are very high risk of CKD progression.

Our results demonstrated that a correlation between 25(OH)D and 1,25(OH)2D was only present in the low and very high risk groups, and not in the moderate risk or high risk groups (Fig. 4). In comparison to the low and very high risk groups, the median 1,25(OH)2D value decreased from 57 to 43 pg/mL. The Passing-Bablok fit was used to analyze the correlation between the 25(OH)D and 1,25(OH)2D levels.

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**Figure 4.** Scatter plots of 25(OH)D vs. 1,25(OH)2D among the four risk progression groups. A: All patients, B: Low risk group, C: Moderate risk group, D: High risk group, E: Very high risk group. The correlation coefficients were 0.31 0.06 0.10 and 0.44 respectively. Linear regression was evaluated using Passing-Bablok-fit. See Figure 1 for the definitions of the abbreviations.
in the low and very high risk groups, and the results showed that the two groups had similar slopes of linear regression (slope = 3.3); however, they had different y-intercepts (9.8 vs. -5.4, respectively). These findings could reflect the weakening of the hydroxylation function, which serves to convert 25(OH)D to 1,25(OH)2D, with the progression of CKD. One plausible explanation for the loss of correlation in the moderate risk and high risk groups is individual differences in the function decline in hydroxylation.

Patients with end-stage CKD should be treated with calcitriol due to their weak 25(OH)D hydroxylation. Furthermore, the serum levels of 25(OH)D should be monitored in patients in the high risk group to facilitate the early detection of any decreases in hydroxylation function. However, medical supplementation with vitamin D and the measurement of 25(OH)D are not covered by the government-based medical insurance system in Japan. Interestingly, none of the patients in the present study received vitamin D supplementation. Further investigation is needed to examine the outcome and the causal relationships of 25(OH)D deficiency.

The present study is associated with certain limitations. The study did not include a control group; instead, we used the low-risk group and a high eGFR group for comparison. In addition, we only tested samples that were collected in winter, when the duration of daylight is short. Another limitation of this study is the small sample size of the G5 group.

Conclusion

In conclusion, this study showed that Japanese patients with diabetic nephropathy and CKD had low vitamin D levels. The significant risk factors for low vitamin D levels included macro-albuminuria, young age, and female gender. The relationship between the 25(OH)D and 1,25(OH)2D levels changed with the progression of CKD. Further studies are needed to determine the best timing for vitamin D supplementation.

The authors state that they have no Conflict of Interest (COI).

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References


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