Association of Fasting Glucose and Glycated Hemoglobin with Vitamin D Level According to Diabetes Mellitus Status in Korean Adults

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Abstract

Background

Previous studies have suggested that vitamin D deficiency might increase the risk of type 2 diabetes mellitus(DM). However, few studies have examined whether vitamin D continues to affect glucose control after DM diagnosis. Therefore, we examined the association between vitamin D and glucose in nondiabetics and DM patients.

Methods

We analyzed data for 32,943 adults aged 19 years and older from the 2008 to 2014 Korea National Health and Nutrition Examination Survey. Vitamin D levels were determined using the 25-hydroxyvitamin D concentration, and patients were grouped into one of three categories according to those results. DM was defined as a fasting glucose level ≥ 126 mg/dL, current use of DM medications or insulin injections, or a self-reported diagnosis of DM by a doctor.

Results

In male DM patients, hemoglobin A1c(HbA1c) level increased significantly as vitamin D levels

became severely deficient. Among the abnormal HbA1c subgroups of males and postmenopausal females, HbA1c levels were significantly higher in the severe vitamin D deficiency subgroup (p for trend = 0.0044 and 0.0219 for males and postmenopausal females, respectively). There were significant differences between abnormal HbA1c subgroups and normal HbA1c subgroups in both males and females. Regardless of sex or menopause status, however, there was no significant association between vitamin D and fasting glucose in fasting glucose subgroups.

Conclusions

Males and females in the abnormal HbA1c subgroups showed markedly elevated blood glucose when they also had vitamin D deficiency. Furthermore, there was a more distinct difference in the HbA1c subgroups than in the fasting glucose subgroups.

Keywords: Diabetes Mellitus, Blood Glucose, Glycated Hemoglobin A1c, Vitamin D, Korea

Introduction

Vitamin D is abundant in externally blue fish and egg yolks (1), but only a small amount of vitamin D intake occurs via food consumption; instead, most is produced by the body upon exposure to sunlight (2). There is increasing interest in vitamin D because vitamin D deficiency has become common, not only in Korea, but also in other countries (3). Low vitamin D levels are associated with mental diseases, cancer, and cardiovascular disease (4-7). Also, some research has shown that vitamin D affects insulin sensitivity and insulin secretion: insulin secretion was reduced in vitamin D-deficient rats, and their insulin levels increased after they received an injection of vitamin D (8). Because vitamin D affects insulin secretion and insulin sensitivity, which are important factors in the development of diabetes mellitus (DM), it is possible that vitamin D levels are linked to the development of DM.

DM is a chronic disease caused by defects in insulin secretion or regulation (9), and the increasing prevalence of DM has become a social and health problem worldwide (10). According to the Korean Diabetes Association, the prevalence of DM among Korean adults older than 30 years in 2018 was 13.8%, which represents an increase to a high prevalence over the past 7 years (11). Furthermore, the International Diabetes Federation reported that DM patients numbered about 463 million in 2019, but that number was expected to increase to about 700 million by 2045 (12). DM causes complications such as stroke, cardiovascular disease, retinopathy, and nephropathy, and it increases the annual mortality rate of patients (13, 14). In addition, DM patients with a longer illness duration

experience greater morbidity and DM-related mortality rates than those with a shorter duration (15, 16). Continuing management of DM produces an ever-growing medical expense burden, such that low-income groups often show poor medical compliance (17, 18).

Previous studies that investigated the association between vitamin D and the development of DM have reported that those with vitamin D deficiency have an increased prevalence of type 2 DM (19, 20). Another study reported that supplementation with vitamin D and calcium decreased fasting glucose in individuals with impaired glucose tolerance (21), indicating that vitamin D can help prevent DM. According to a recent meta-analysis of DM patients, vitamin D supplementation decreased insulin resistance compared with a placebo group, but it had no effect on fasting glucose or hemoglobin A1c (HbA1c) (22). Few studies have investigated the association between vitamin D levels and glucose control among Korean DM patients.

Although many studies have sought to establish the association between vitamin D and DM, only a few studies have included Korean patients with DM. Also, the mechanism by which vitamin D affects glucose control in DM patients is unclear. Therefore, in this study, we examined differences in the associations between vitamin D levels and glucose in DM patients and nondiabetics by using data from the Korea National Health and Nutrition Examination Survey (KNHANES) from 2008 to 2014.

Methods

Study population

This study used data from KNHANES, a study initiated in 1998; the data from KNHANES VIII (2019-) remain in progress. We used data from the second period of KNHANES IV (2008) to the second period of KNHANES VI (2014), which included 25-hydroxyvitamin D, abbreviated as 25(OH)D, concentration results for participants. Among the 61,379 participants, we excluded those younger than 19 years ($n = 14,620$), those who had missing serum 25(OH)D values ($n = 12,137$), and those who had missing values concerning the definition of DM ($n = 1,679$). Therefore, we analyzed data from 32,943 participants.

Demographic and lifestyle information

The general characteristic variables of the study participants were age, sex, total energy intake, education level, household income level, smoking status, obesity, and physical activity. Total energy intake was calculated as the total daily calories consumed by each person as reported using a 24-hour recall method. Education level was divided into four categories (< elementary school graduates, middle school graduates, high school graduates, $\geq$ college graduates), and household income level was divided into quartiles according to equivalized income (total household income divided by the square root of the number of household members). Smoking status was stratified as current smoker, previous smoker, and never smoker. Obesity was stratified into three categories after calculating the body mass index (BMI) from height and weight. According to the World Health Organization's

criteria for the Asian population, the BMI cutoff values for underweight and obese individuals are less than 18.5 kg/m² and at least 25 kg/m², respectively (23). Participants who performed moderate physical activity for at least 30 min/d on 5 d/week or vigorous physical activity for at least 20 min/d on 3 d/week were assigned to the high exercise level subgroup; others were assigned to the low exercise level subgroup.

Measurement of vitamin D levels

The serum 25(OH)D concentration was measured by radioimmunoassay using a 25(OH)D 125I radioimmunoprecipitation assay kit and a 1470 WIZARD gamma-counter (PerkinElmer, Waltham, MA, USA). Vitamin D levels were divided into three categories: patients in the severe deficiency subgroup had a 25(OH)D concentration of less than 10.0 ng/mL, those in the deficiency subgroup had a 25(OH)D concentration of 10.0 ng/mL to 20.0 ng/mL, and those in the sufficient subgroup had a 25(OH)D concentration greater than 20.0 ng/mL (24, 25).

Definition of DM and blood glucose status criteria

All of our study participants had blood testing results from samples taken following a fast of longer than eight hours. DM patients were defined as those with a fasting glucose level $\geq$ 126 mg/dL, current use of DM medication or insulin injections, or a self-reported diagnosis of DM by a doctor.

Participants were sub-grouped using an HbA1c concentration of 6.5% and a fasting glucose level of 126 mg/dL for the blood glucose status analyses (26).

Statistical analysis

All statistical analyses involved a complex survey design, sampling weights, and stratified and clustered sampling. The chi-square test was applied to categorical variables to estimate the frequencies and percentages of the characteristics of participants according to their vitamin D levels. Differences in continuous variables among the vitamin D level subgroups were assessed by a one-way analysis of variance to estimate the means and standard errors, followed by Tukey's multiple comparison test.

To determine whether vitamin D showed different association with DM, we ran a multiple linear regression analysis stratified according to the prevalence of DM and to glucose levels. Age, sex, total energy intake, education level, smoking status, obesity, and physical activity were considered as confounding factors. Also, we conducted interaction tests to confirm whether the differences in the associations between normal and abnormal glucose levels were significant. The dependent variables were fasting glucose and HbA1c, which are both continuous variables. DM status, fasting glucose divided by cutoff, and HbA1c divided by cutoff, which are categorical variables, were used as interaction variables. For normality, fasting blood glucose and HbA1c levels were analyzed by log transformation, and the relevance was compared according to sex and menopause status. All

analyses were conducted using SAS (Statistical Analysis System version 9.4, SAS Institute, Cary, NC, USA), and significance was defined as a two-tailed P -value less than 0.05.

Results

Among the 32,943 study participants, the mean age was 44.15 years, and the mean serum 25(OH)D concentration was 17.53 ng/mL. The general characteristics of participants according to their vitamin D levels are shown in Table 1. Overall, 2,650 (8.62%) participants were classified into the severe deficiency subgroup, 19,633 (61.60%) were classified into the deficiency subgroup, and 10,660 (29.78%) were classified into the sufficient subgroup. Participants in the severe deficiency or deficiency subgroups had significantly lower ages, total energy intake, proportion of current smokers, and rates of obesity and physical activity than those in the sufficient subgroup ($P < 0.0001$). In the severe deficiency subgroup, on the other hand, education level was significantly higher than in the other subgroups, and the proportion of females was highest ($P < 0.0001$). The prevalence of DM was highest in the sufficient subgroup ($P < 0.0001$).

The results of our analysis of the association between vitamin D levels and fasting glucose after stratification by DM status are shown in Table 2. Among DM patients, both fasting glucose and HbA1c levels were significantly higher in the severe vitamin D deficiency subgroup than in the sufficient subgroup (P for trend = 0.0123 and 0.0002 for fasting glucose and HbA1c, respectively),

whereas those values did not correlate significantly in the nondiabetic study population. Additionally, in the analyses stratified by the cutoff value for fasting glucose (126 mg/dL), we found a significant inverse association between vitamin D and fasting glucose or HbA1c in the abnormal fasting glucose level subgroup (P for trend = 0.0321 and 0.0008 for fasting glucose and HbA1c, respectively) but no significant association in the normal fasting glucose subgroup. In the analyses stratified by the HbA1c cutoff value (6.5%), we found a significant inverse association between vitamin D and glucose control in the abnormal subgroup (P for trend = 0.0116 and 0.0002 for fasting glucose and HbA1c, respectively), and a significant association between vitamin D and fasting glucose in the normal HbA1c level subgroup (P for trend = 0.0338).

To confirm whether the association with vitamin D differed according to sex or menopause status, we conducted stratified analyses. In males, the HbA1c level increased significantly as vitamin D became severely deficient in DM patients and in the abnormal fasting glucose and abnormal HbA1c subgroups (P for trend = 0.0003, 0.0006, and 0.0044 for DM patients, abnormal fasting glucose subgroup, and abnormal HbA1c subgroup, respectively), whereas there was no significant association between vitamin D and fasting glucose in any normal subgroup (Table 3). In females, there was a significant association between vitamin D levels and fasting glucose and HbA1c in the abnormal HbA1c subgroup (P for trend = 0.0041 and 0.0050 for fasting glucose and HbA1c, respectively) (Table 4). Table 5 shows that before menopause, there was a significant association between vitamin D and glucose control in the normal HbA1c subgroup, but there were no significant

differences between abnormal HbA1c subgroups and normal subgroups (P for interaction = 0.3892).

After menopause, however, the fasting glucose level increased significantly in DM patients and those in the abnormal HbA1c subgroup. Also, the HbA1c level was significantly higher in the abnormal HbA1c level subgroup (Table 6). Regardless of sex or menopause status, there was no significant association between vitamin D and glucose levels in nondiabetic populations.

In the logistic regression, we found no significant association between vitamin D and DM risk before menopause (Supplement 1). Even when stratified by supplements or daily calcium intake to confirm the independent association between calcium intake and vitamin D, the association between vitamin D and DM risk was significant only in DM patients (Supplement 2).

Discussion

Males and females in the abnormal HbA1c subgroup showed markedly elevated blood glucose when they also had vitamin D deficiency. Furthermore, there was a more distinct difference in HbA1c subgroups than in fasting glucose subgroups.

In humans, 7-dehydrocholesterol present in the skin is converted to pre-vitamin D₃ by ultraviolet rays and then into vitamin D₃ deeper in the body (27). Vitamin D₃ is combined with vitamin D-binding protein synthesized in the liver to become 25(OH)D, which is hydroxylated by 1 α -hydroxylase in the kidney to become 1,25-dihydroxyvitamin D (1,25(OH)₂D₃) (28). Vitamin D

receptors and vitamin D–dependent calcium-binding proteins are present in pancreatic β -cells and can affect insulin secretion and insulin sensitivity (29). Vitamin D affects insulin action by regulating the extracellular calcium that maintains the influx of normal calcium through the cell membrane and controlling the appropriate intracellular cytoplasmic calcium $[Ca^{2+}]$ pool (30). Therefore, when vitamin D is insufficient, parathyroid hormone (PTH) can increase, which elevates the concentration of free intracellular Ca^{2+} in insulin-responsive tissues, including skeletal muscle and adipose tissue. That can deform the balance between the intracellular and extracellular β -cell calcium pools, disturbing the normal insulin secretion in response to glucose (31). Also, PTH is associated with insulin resistance, and one study showed that PTH decreased the glucose absorption stimulated through insulin in rat adipocytes (32). In other words, PTH can cause insulin resistance by decreasing the amount of GLUT1 and GLUT4 in cell membranes (33). Thus, PTH promotes insulin resistance by reducing glucose absorption in the liver, muscle, and adipose tissue (34). However, the mechanism involved has not yet been clarified.

A meta-analysis of recent studies confirmed an association between vitamin D supplementation and fasting glucose in nondiabetics, but vitamin D did not generally show a significant association with the fasting glucose level; only the subgroup of participants with a BMI <25 kg/m² and the subgroup with a 25(OH)D concentration in the range of 20.0 ng/mL to 30.0 ng/mL showed a significant decrease in fasting glucose (35). This is consistent with our results in this study, which show no significant association between vitamin D and fasting glucose or HbA1c in nondiabetics. In contrast,

a meta-analysis of observational studies confirmed the association between vitamin D deficiency and type 2 DM and reported a significant inverse association between vitamin D and glucose levels in both DM patients and nondiabetics (36). However, most of the studies included in that meta-analysis were conducted in other countries; few studies have focused on Koreans.

Many studies have considered glucose control in DM patients, but their results have been inconsistent. According to a recent meta-analysis of type 2 DM patients, their fasting glucose, HbA1c, and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) scores all decreased significantly with vitamin D supplementation of at least 4,000 IU per day (37). On the other hand, another meta-analysis published in the same year reported finding insufficient evidence to indicate that glucose metabolism or insulin improved in DM patients following supplementation with vitamin D (38). Among the studies included in the latter meta-analysis, a significant decrease in both glucose and HOMA-IR score was observed in patients treated with 1,000 IU of vitamin D and 300 mg of calcium (39). However, most studies included in both meta-analyses of DM patients were conducted outside Korea; a study of Koreans did not demonstrate significant changes following vitamin D and calcium supplementation (40). One reason for that result was that only about 44% of those who received vitamin D and calcium reached target vitamin D levels.

Because DM is a chronic disease with a high risk of complications, continuous blood glucose control is important (26). However, according to a 2020 DM fact sheet published by the Korean Diabetes Association, only about 28.3% of DM patients in Korea control their HbA1c concentration to less

than 6.5%, and 19.1% of patients had an HbA1c concentration greater than 8.0% (11). An international cross-sectional study confirmed an inverse association between HbA1c and the serum 25(OH)D concentration in DM patients after adjusting for DM severity (41). In addition, a study confirming the association between the HbA1c regulation rate and vitamin D deficiency in DM patients in Pakistan reported greater vitamin D deficiencies in DM patients whose HbA1c concentrations were 7.0% or higher (42). Those previous studies suggest that vitamin D plays an important role in controlling blood glucose in DM patients.

Therefore, we conducted stratified analyses according to DM status and glucose levels to determine whether the role of vitamin D differs between DM prevention and progression. We found a significant association between vitamin D and glucose control in the abnormal HbA1c subgroups of males and postmenopausal females. Therefore, we assume that vitamin D is more valuable as a prognostic factor among DM patients whose glucose is high than as a preventive factor among nondiabetics. Premenopausal females in the normal HbA1c subgroup showed a significant association between vitamin D and glucose control, indicating that estrogen is associated with glucose control in that population. One study showed that most postmenopausal people face a dramatic increase in insulin resistance (43). Estrogen might regulate insulin through insulin-sensitive tissues or by regulating factors such as oxidative stress that contribute to insulin resistance (44).

This study has some limitations and strengths. First, this study was a cross-sectional study, so we cannot comment on the causal relationship between vitamin D levels and DM status. Second, we

did not consider the exposure time and irradiation season, which could affect vitamin D levels. However, to consider those factors as much as possible, we did perform our statistical analyses after adjusting for confounders. Third, we could not classify or analyze the type of DM because KNHANES does not distinguish between type 1 and type 2 DM. However, because type 1 DM occurs mostly in childhood and has a low prevalence (45), it can be assumed that most DM patients included in this study had type 2 DM. Also, although the KNHANES data do not include information about the level of dietary vitamin D, the serum 25(OH)D level used in this study reports both the vitamin D concentration produced by synthesis in the skin and dietary vitamin D intake (46). This study has the strengths of representing Korean adults by using KNHANES data and analyzing the relationship between vitamin D and blood glucose in both DM patients and nondiabetics, which allowed us to confirm the differences in associations between vitamin D and blood glucose control according to DM status. Because our results confirm the relationship between vitamin D and blood glucose, and most of the Koreans in our study population had relatively insufficient vitamin D levels, this work could be used to prepare management guidelines for blood glucose control.

In conclusion, we found a difference in the association between vitamin D and glucose control according to DM status in Korean adults. Few studies have confirmed an association between vitamin D and glucose control in Koreans. Guidelines are needed for managing glucose control in DM patients that reflect the results of this research performed among Koreans. Additional large-scale longitudinal studies should be conducted to clarify the causal relationships in this association.

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Table 1. Characteristics of subjects by vitamin D level

Characteristics	Sufficiency ≥20.0 ng/mL	Deficiency 10.0-19.9 ng/mL	Severe deficiency <10.0 ng/mL	p-value ¹
N	10660	19633	2650	
25(OH)D (ng/dL)	25.35±0.08	15.03±0.04	8.42±0.04	<.001
Age (years)	48.59±0.26 ^a	42.53±0.17 ^b	40.36±0.39 ^c	<.001
Sex [n (%)]				
Male	5721 (60.76)	7818(47.96)	727 (35.50)	<.001
Female	4939 (39.24)	11815 (52.04)	1923 (64.50)	
Total energy intake (Kcal/day)	2108.63±13.79 ^a	2013.87±10.03 ^b	1843.22±22.04 ^c	<.001
Education level [n (%)]				
≤Elementary school graduation	3429 (23.39)	4163 (14.59)	527 (13.71)	<.001
Middle school graduation	1438 (12.73)	1904 (8.76)	231 (7.60)	
High school graduation	3237 (36.24)	7175 (41.40)	1035 (44.77)	
≥College graduation	2526 (27.64)	6362 (35.25)	851 (33.92)	
Household income level [n (%)]				
Low	2422 (17.25)	3173 (13.25)	456 (15.75)	<.001
Low-middle	2674 (26.12)	4885 (25.92)	713 (27.44)	
High-middle	2672 (27.67)	5593 (30.46)	752 (29.99)	
High	2772 (28.95)	5743 (30.37)	682 (26.81)	
Smoking status [n (%)]				
Never	5520 (46.97)	12024 (55.44)	1809 (62.06)	<.001
Former	1510 (15.56)	2325 (12.76)	212 (8.56)	
Current	3608 (37.47)	5250 (31.80)	622 (29.37)	
Obesity [n (%)]				
Underweight (<18.5 kg/m ²)	386 (3.49)	877 (4.82)	216 (8.91)	<.001
Normal (18.5 to <25 kg/m ²)	6728 (63.23)	12449 (63.45)	1717 (65.39)	
Obese (≥25 kg/m ²)	3496 (33.29)	6192 (31.74)	678 (25.70)	
Physical activity [n (%)]				
No	7749 (71.37)	15076 (75.61)	2109 (77.43)	<.001
Yes	2871 (28.63)	4498 (24.39)	530 (22.57)	
Fasting glucose level (mg/dL)	97.88±0.25 ^a	96.14±0.19 ^b	95.68±0.61 ^b	<.001
HbA1c (%)	5.90±0.02 ^a	5.77±0.01 ^b	5.80±0.04 ^{ab}	<.001
Diabetes mellitus [n (%)]				
No	9456 (90.22)	17832 (92.62)	2378 (91.88)	<.001
Yes	1204 (9.78)	1801 (7.38)	272 (8.12)	

Values are presented as mean±standard error or n (%); Different letters represent statistically significant differences by Tukey's multiple comparison test.

¹P-values were derived from a chi-square test for categorical variables and from generalized linear regression analysis for continuous variables.

Table 2. Association of vitamin D with log(fasting glucose) and log(HbA1c) by diabetes status or glucose level

Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(fasting glucose)		0.0009	log(fasting glucose)		0.0030	log(fasting glucose)		0.0034
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0297*	0.0014		0.0172	0.0007		0.0315*	0.0039	
Severe deficiency (<10 ng/mL)	0.0466	0.0012		0.0571	0.0007		0.0633	0.0105*	
p-trend	0.0123	0.4724		0.0321	0.7116		0.0116	0.0338	
Vitamin D level	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(HbA1c)		<0.0001	log(HbA1c)		<0.0001	log(HbA1c)		<0.0001
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0291**	0.0007		0.0297**	-0.0008		0.0251**	0.0010	
Severe deficiency (<10 ng/mL)	0.0645**	0.0009		0.0795**	0.0020		0.0689**	0.0008	
p-trend	0.0002	0.7188		0.0008	0.7938		0.0002	0.6507	

Values are β.

Adjusted for age, sex, total energy intake, education level, smoking status, obesity, and physical activity.

*P-value<0.05; **P-value<0.01

Table 3. Association of vitamin D with log(fasting glucose) and log(HbA1c) by diabetes status or glucose level in males

Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(fasting glucose)		0.0416	log(fasting glucose)		0.0656	log(fasting glucose)		0.1613
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0287	0.0022		0.0142	0.0016		0.0353	0.0029	
Severe deficiency (<10 ng/mL)	0.0535	-0.0006		0.0890	-0.0009		0.0329	0.0084	
p-trend	0.0917	0.6233		0.0859	0.7590		0.1849	0.2991	
Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(HbA1c)		0.0001	log(HbA1c)		0.0005	log(HbA1c)		0.0027
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0365**	0.0003		0.0392**	-0.0007		0.0344**	0.0011	
Severe deficiency (<10 ng/mL)	0.1063**	-0.0012		0.1368**	0.0021		0.0756	-0.0035	
p-trend	0.0003	0.9256		0.0006	0.9229		0.0044	0.8315	

Values are β.

Adjusted for age, total energy intake, education level, smoking status, obesity, and physical activity.

*P-value<0.05; **P-value<0.01

Table 4. Association of vitamin D with log(fasting glucose) and log(HbA1c) by diabetes status or glucose level in females

Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(fasting glucose)		0.0098	log(fasting glucose)		0.0566	log(fasting glucose)		0.0026
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0357	0.0012		0.0263	0.0001		0.0409	0.0065	
Severe deficiency (<10 ng/mL)	0.0432	0.0023		0.0435	0.0016		0.0980**	0.0138**	
p-trend	0.0795	0.4367		0.1179	0.6779		0.0041	0.0079	
Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(HbA1c)		0.0113	log(HbA1c)		0.0798	log(HbA1c)		0.0013
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0187	0.0006		0.0160	-0.0013		0.0183	0.0007	
Severe deficiency (<10 ng/mL)	0.0307	0.0024		0.0382	0.0025		0.0641**	0.0036	
p-trend	0.1110	0.5352		0.1610	0.7131		0.0050	0.3261	

Values are β.

Adjusted for age, total energy intake, education level, smoking status, obesity, and physical activity.

*P-value<0.05; **P-value<0.01

Table 5. Association of vitamin D with log(fasting glucose) and log(HbA1c) by diabetes status or glucose level in pre-menopausal females

Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(fasting glucose)		0.9209	log(fasting glucose)		0.5643	log(fasting glucose)		0.3892
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0163	0.0022		-0.0190	0.0029		-0.0100	0.0128**	
Severe deficiency (<10 ng/mL)	0.0311	0.0040		0.0168	0.0045		0.0830	0.0183**	
p-trend	0.7361	0.2928		0.9035	0.2238		0.5312	0.0047	
Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(HbA1c)		0.3571	log(HbA1c)		0.5192	log(HbA1c)		0.0483
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0195	0.0004		-0.0009	0.0016		0.0312	0.0011	
Severe deficiency (<10 ng/mL)	0.0608	0.0010		0.04466	0.0026		0.1126*	0.0026	
p-trend	0.3329	0.8246		0.5510	0.5751		0.0586	0.5540	

Values are β.

Adjusted for age, total energy intake, education level, smoking status, obesity, and physical activity.

*P-value<0.05; **P-value<0.01

Table 6. Association of vitamin D with log(fasting glucose) and log(HbA1c) by diabetes status or glucose level in post-menopausal females

Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(fasting glucose)		0.0280	log(fasting glucose)		0.1342	log(fasting glucose)		0.0171
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0414*	0.0008		0.0321	-0.0024		0.0483*	0.0023	
Severe deficiency (<10 ng/mL)	0.0471	0.0014		0.0401	-0.0003		0.0911*	0.0140	
p-trend	0.0389	0.7611		0.1129	0.6569		0.0035	0.3433	
Vitamin D levels	Diabetes	Nondiabetes	P for interaction	Fasting glucose abnormal	Fasting glucose normal	P for interaction	HbA1c abnormal	HbA1c normal	P for interaction
	log(HbA1c)		0.1236	log(HbA1c)		0.2583	log(HbA1c)		0.0461
Sufficiency (≥20 ng/mL)	Ref	Ref		Ref	Ref		Ref	Ref	
Deficiency (10 to <20 ng/mL)	0.0200	0.0016		0.0191	-0.0041		0.0149	0.0007	
Severe deficiency (<10 ng/mL)	0.0252	0.0083		0.0304	0.0080		0.0524*	0.0086	
p-trend	0.1485	0.2748		0.2385	0.9112		0.0219	0.2218	

Values are β.

Adjusted for age, total energy intake, education level, smoking status, obesity, and physical activity.

*P-value<0.05; **P-value<0.01

Figure 1. Flow chart of study participant selection from the 2008 to 2014 Korea National Health and Nutrition Examination Survey (KNHANES)