Lack of correlation between serum 25(OH)D level and endoscopy-based chronic rhinosinusitis in Korean adults*

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Background: Several previous studies have shown that serum 25(OH)D deficiency is associated with increased risk of chronic rhinosinusitis (CRS) in adults and also correlated with disease severity. We aimed to investigate the correlation between serum 25(OH)D level and endoscopy-based CRS in adults using the Korean National Health and Nutrition Examination Survey.

Methods: The data were based on the Korean National Health and Nutrition Examination Survey from 2008 to 2011. Diagnosis of endoscopy-based CRS was based on endoscopic findings of mucopurulent rhinorrhea in the middle meatus or nasal polyps, with nasal symptoms satisfying symptom-based CRS based on European Position Paper on Rhinosinusitis and Nasal Polyps 2012 criteria. Nasal symptoms included nasal obstruction, anterior/posterior nasal drip, facial pain, and the loss of smell. Serum 25(OH)D level was defined as deficient (<20 ng/mL), insufficient (20–29.9 ng/mL), or sufficient (≥30 ng/mL).

Results: The serum 25(OH)D level in the CRS group was 19.293 ± 7.035 ng/mL, which was higher than that of the control group (18.057 ± 6.56 ng/mL, p = 0.0072). Among symptom combinations of endoscopy-based CRS, some combinations with mucopurulent rhinorrhea at the middle meatus were significantly related to normal serum 25(OH)D level.

Conclusion: Low serum 25(OH)D level might not be associated with increased prevalence of CRS in Korean adults; rather, patients with CRS showed higher serum 25(OH)D levels than the control group. Thus, these results, contradicting those of previous studies, should be further verified in other countries to investigate the role of the serum 25(OH)D in CRS.

Key words: epidemiology, rhinosinusitis, 25(OH)D, endoscopy, mucopurulent rhinorrhea, nasal polyp

Introduction

Beyond its pivotal role in bone mineralization, recent studies have shown that 25(OH)D deficiency is associated with an increase in upper airway diseases such as allergic rhinitis and asthma[1-3]. Nutritional studies in pregnancy indicate that increasing maternal consumption of 25(OH)D decreases the risk of asthma in newborn babies, suggesting that *in utero* exposure to 25(OH)D might activate protective mechanisms in the developing immune system[4]. There is increasing evidence indicating that 25(OH)D supplementation in people who are 25(OH)D deficient can provide protection against respiratory infection[5,6]. Through its effects on the immune system, serum 25(OH)D could play an important role in the pathogenesis of upper airway diseases such as chronic sinusitis.

Chronic rhinosinusitis (CRS) is one of the most prevalent chronic diseases, characterized by the inflammation of the paranasal sinus mucosa for 12 consecutive weeks or more. Although insights into the pathogenesis of CRS have largely expanded over recent years, the exact etiology and mechanism are still unknown. Not only does 25(OH)D support immune function, regulate cell growth, and help reducing inflammation, but several recent reports have also shown a link between the increase of CRS and 25(OH)D deficiency[7-9]. In some studies, serum 25(OH)D levels were found to be lower in patients with CRS and to correlate with disease severity[9]. However, these previous studies were conducted only in Western populations and included small

sample sizes, which may have influenced the results and its significance. Therefore, the aim of this study was to investigate the association between serum 25(OH)D level and CRS diagnosed with endoscopy-based European Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS) 2012 criteria using the data from the 2008 to 2011 Korean National Health and Nutrition Examination Survey (KNHANES) in adults from South Korea.

Materials and methods

Subjects and survey methods

KNHANES is a complex survey because the data were not obtained using a simple random sample. Rather, a complex, multistaged, probability sampling design was used to select participants. Within the visiting survey team, a resident of the Korean Society of Otorhinolaryngology-Head & Neck Surgery was included. At least second-year residents of the Korean Society of Otorhinolaryngology-Head & Neck Surgery performed the endoscopic examinations. Standardization of the endoscopic examinations in KNHANES was performed as previously described[10]. Baseline information for each population was obtained using a structured questionnaire administered by trained interviewers. After the baseline survey, the residents asked more specific questions on the questionnaire concerning the following nasal symptoms: mucopurulent discharge, nasal obstruction/congestion, facial pain/pressure, and dysosmia lasting longer than 3 months. At the same time, the residents performed a physical examination on individuals aged 12 years or older using a 4-mm, 0° rigid nasal endoscope in a well-equipped mobile medical examination bus. Nasal endoscopic examination was performed 5 minutes after applying a topical vasoconstrictor (0.5% Neo-Synephrine : distilled water = 1 : 1).

Informed consent and Ethics Committee Review approval

This study was reviewed and approved by the Institutional Review Board (IRB) in accordance with the Helsinki Declaration. The survey protocol was approved by the IRB of the Korea Centers for Disease Control and Prevention. The IRB approval numbers are 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, and 2011-02CON-06-C.

Definition of CRS

We assessed the prevalence of CRS based on the diagnostic criteria of endoscopy-based CRS. The diagnosis of endoscopy-based CRS was done as a diagnosis based on endoscopic findings of mucopurulent rhinorrhea in the middle meatus (AF1) or nasal polyps (AF2), with nasal symptoms meeting the definition criteria of symptom-based CRS. For endoscopic examination, AF1 was defined as mucopurulent rhinorrhea at middle meatus, and AF2 was defined as nasal polyp in the nasal cavity. AF3 was defined as other tumors except nasal polyp. We included AF1 and AF2 for the diagnosis of endoscopy-based CRS. The questionnaires assessed symptoms such as nasal blockage or obstruction or congestion, anterior/posterior nasal drip, facial pain, and loss of smell. Symptom-based CRS was defined using the EP3OS 2012 diagnostic criteria for epidemiological studies (Table 1).

Table 1. Definition of CRS based on different diagnostic criteria.

Symptom-based CRS
Inflammation of the nose and the paranasal sinuses characterized by two or more symptoms, one of which should be either
nasal blockage / obstruction / congestion or nasal discharge (anterior/posterior nasal drip)
± facial pain/pressure
± reduction or loss of smell
Duration of symptoms > 12 weeks
Endoscopy-based CRS
Endoscopic findings of mucopurulent rhinorrhea (AF1) or nasal polyps (AF2)
and
Nasal symptoms meeting the criteria of symptom-based CRS

CRS = chronic rhinosinusitis

Measurement of serum 25(OH)D level

Blood samples were obtained after a 12-h overnight fast. The serum 25(OH)D level was measured by radioimmunoassay using a 25(OH)D 125I radioimmunoassay kit (DiaSorin, Stillwater, Oklahoma, USA). The radioimmunoassay was performed with the 1470 WIZARD gamma counter (PerkinElmer, Turku, Finland). Subjects were categorized into three groups according to serum 25(OH)D level. Serum 25(OH)D levels below 20 ng/mL (50 nmol/L) were defined as deficiency, levels ranging from 20 to 29.9 ng/mL (50–74 nmol/L) were defined as insufficiency, and levels above 30 ng/mL (75 nmol/L) were defined as sufficiency according to the criteria of the endocrine society[11].

Demographic factors

The statistical association between 25(OH)D level and demographic factors was analyzed. Demographic factors included clinically relevant sociodemographic and personal medical factors. The factors we considered were based on previous epidemiological studies regarding CRS, from which we chose 11 variables. Factors included sex, age, smoking, education, stress, obesity, hypertension, diabetes mellitus, bronchial asthma, allergic rhinitis, and stroke. Additionally, we added calcium intake, cholesterol level, and HbA1c level. Age, calcium intake, cholesterol level, and HbA1c level were set as numerical variables, and the other factors were set as categorical variables. All variables were defined based on the answers to the questionnaire and the blood chemistry data (Table 2). The details for categorizing each factor and the diagnosis of each disease were described previously[10].

Table 2. Definition of factors applied in the analysis.

Variables	Definitions
Sex	Male / female
Age	Based on American age
Smoking	(-): former smokers or nonsmokers
	(+): current smokers
Obesity	(-) or (+): based on BMI
Education	Low: graduated middle & high school
	High: graduated university
Stress	Light or heavy: subjective feelings of stress in daily life
Hypertension	(-) or (+): history of hypertension diagnosed by a doctor
Diabetes mellitus	(-) or (+): history of diabetes mellitus diagnosed by a doctor
Stroke	(-) or (+): history of stroke diagnosed by a doctor
Bronchial asthma	(-) or (+): history of bronchial asthma diagnosed by a doctor
Allergic rhinitis	(-) or (+): history of allergic rhinitis diagnosed by a doctor
Calcium intake	The amount of calcium intake / 1day (mg)
Cholesterol	Based on enzyme method
HbA1c	Based on high performance liquid chromatography

Statistical analysis

To estimate the entire non-institutionalized Korean population from the survey sample, the KNHANES sampling weight variables, masked variance primary sampling unit, and stratum variables were used. Survey sample weights were used in all analyses. The data were analyzed with SAS software (version 9.2, SAS Institute Inc., Cary, NC, USA) in order to incorporate sample weights and adjust the analysis for the complex sample design of the survey. The prevalence of CRS based on diagnostic criteria was estimated, and the differences of serum 25(OH)D level between each group were statistically analyzed using the independent two-sample t-test and chi-square test as appropriate. While the independent two-sample t-test was performed using 25(OH)D level as a continuous variable, the chi-square test was performed using 25(OH)D level as a categorical variable. Univariate cumulative logistic regression (clogit) analysis was performed with the 25(OH)D level variable to calculate adjusted odds ratios (ORs) and their 95% confidence intervals (CIs). To perform cumulative logistic regression, we formed two groups according to 25(OH)D level: the normal group included sufficient and insufficient 25(OH)D groups, and the abnormal group included the deficient 25(OH)D group. The analysis was performed on each CRS diagnostic criteria set. After univariate logistic regression, multivariate logistic regression using stepwise selection method was performed to confirm significant variables. A p-value < 0.05 was considered statistically significant.

Results

Demographic data

A total of 30,609 individuals aged 19 years or older from 38,638 paricipants in 4,000 households was chosen in the KNHANES from January 2008 to December 2011, and these randomly selected participants represented the general population of South Korea. The male-to-female ratio was 1:1.32, and the mean age was 49.85 ± 16.78 years. There were 1,712 subjects in the 25(OH)D sufficient group, 8,412 in the 25(OH)D insufficient group, and 20,485 in the 25(OH)D deficient group according to 25(OH)D level. An endoscopy-based diagnosis of CRS was done for 645 subjects (2.11% of total subjects). We evaluated the possible effects of demographic factors on serum 25(OH)D level, and all factors except bronchial asthma showed statistically significant difference for three groups (Table 3). We ran univariate logistic regression on all of the confounding factors, and found that all variables were significant. After multivariate logistic regression using stepwise selection method, we identified that female sex, low age, and allergic rhinitis were significant factors showing lower 25(OH)D levels (Table 4).

Comparison of 25(OH)D level between CRS group and control group

When considering serum 25(OH)D level as a continuous variable, the serum 25(OH)D level in the CRS group was 19.29 ± 7.04 ng/mL, which was significantly higher than that of the control group (18.06 ± 6.56 ng/mL; $p = 0.0072$; Figure 1A). Based on the endoscopic examination, the CRS group could divided into the two phenotypes and the serum 25(OH)D level was 18.95 ± 0.71 ng/mL on CRS without nasal polyp and 19.35 ± 1.21 ng/mL on CRS with nasal polyp, respectively (Figure 1B). There was no statistical difference for 25(OH)D level between CRS with nasal polyp and CRS without nasal polyp. As a categorical variable, sufficient serum 25(OH)D level was present in 9.76% of the CRS group compared to 5.57% of the normal group ($p = 0.0054$). Among deficient and insufficient serum 25(OH)D groups, the serum 25(OH)D level showed no significant difference between the CRS group and the control group. However, among sufficient serum 25(OH)D groups, the CRS group showed significantly higher 25(OH)D level than the control group ($p = 0.0242$; Figure 1C).

Relationship between serum 25(OH)D level and the symptoms and signs of endoscopy-based CRS

The serum 25(OH)D levels and all possible CRS symptom combinations were analyzed to identify relationships. The combinations including mucopurulent rhinorrhea at the middle meatus showed generally higher ORs with reliable p-values and had greater power of prediction for normal serum 25(OH)

Table 3. Demographic information tum and NFIM (n=75).

	Total (N=30609)	I (<20ng/mL) (N=20485)	II (≥20ng/mL) (N=8412)	III (≥30ng.mL) (N=1712)	p-value
Vitamin D	18.065±6.564	14.364±3.362	23.818±2.724	34.089±3.914	<.0001*
Sex (n, %)					<.0001*
Male	13177(43.05)	7748(37.82)	4436(52.73)	993(58)	
Female	17432(56.95)	12737(62.18)	3976(47.27)	719(42)	
Age (y)	49.847±16.78	47.435±16.39	53.079±15.66	56.803±14.71	<.0001*
Smoking status, %					<.0001*
former/nonsmoker	6275(50.41)	3657(48.15)	2159(54.42)	459(51.75)	
Current	6174(49.59)	3938(51.85)	1808(45.58)	428(48.25)	
Obesity					<.0001*
(-)	20770(68.35)	14025(69.04)	5529(66.09)	1216(71.28)	
(+)	9617(31.65)	6290(30.96)	2837(33.91)	490(28.72)	
Education					<.0001*
Low	14886(49.40)	9777(48.52)	4210(50.78)	899(53.13)	
High	15249(50.60)	10375(51.48)	4081(49.22)	793(46.87)	
Stress					<.0001*
Light	8290(27.58)	5806(28.89)	2081(25.11)	403(23.90)	
Heavy	21776(72.42)	14287(71.1)	6206(74.89)	1283(76.10)	
Hypertension					0.0003*
(-)	28787(95.63)	19162(95.29)	7992(96.31)	1633(96.29)	
(+)	1316(4.37)	947(4.71)	306(3.69)	63(3.71)	
Diabetes mellitus					<.0001*
(-)	27685(91.96)	18630(92.64)	7535(90.81)	1520(89.62)	
(+)	2420(8.04)	1481(7.36)	763(9.19)	176(10.38)	
Stroke					<.0001*
(-)	29500(97.99)	19757(98.24)	8095(97.55)	1648(97.23)	
(+)	604(2.01)	354(1.76)	203(2.45)	47(2.77)	
Bronchial Asthma					0.0533
(-)	28814(95.71)	19283(95.88)	7923(95.48)	1608(94.81)	
(+)	1291(4.29)	828(4.12)	375(4.52)	88(5.19)	
Allergic rhinitis					0.0015*
(-)	26306(95.13)	17386(94.81)	7390(95.86)	1530(95.27)	
(+)	1346(4.87)	951(5.19)	319(4.14)	76(4.73)	
Ca intake / day	490.245±339.548	487.236±346.223	509.014±337.577	500.204±349.682	<.0001*
Cholesterol	188.509±36.345	187.667±36.602	190.153±35.459	188.577±35.409	<.0001*
HbA1c	5.995±1.113	5.948±1.109	6.063±1.076	6.242±1.028	<.0001*

* Statistically significant ($p < 0.05$).

D level than other combinations. These combinations included mucopurulent rhinorrhea at the middle meatus on endoscopic finding with the following symptoms: anterior/posterior nasal drip and facial pain, anterior/posterior nasal drip and loss of smell, nasal obstruction and anterior/posterior nasal drip and loss of smell, anterior/posterior nasal drip and facial pain and loss of smell, and nasal obstruction and anterior/posterior nasal drip and facial pain and loss of smell (Figure 2, Table 3). Unlike mucopurulent rhinorrhea at the middle meatus on endoscopic exam, the combinations including nasal polyp on endoscopic examination did not show significant ORs relevant to serum 25(OH)D level.

Discussion

CRS is a common condition affecting 6.95% of the adult population, in which the sinuses become inflamed status for at

Table 4. Logistic regression of demographic factors.

Variable	Univariable				Multivariable (Stepwise)			
	OR	95% CI		p-value	OR	95% CI		p-value
Sex (n, %)								
Female vs Male	0.526	0.502	0.552	<.0001	0.526	0.5	0.553	<.0001
Age (y)	1.025	1.023	1.026	<.0001	1.025	1.024	1.027	<.0001
Smoking status, %								
Current vs former/nonsmoker	0.808	0.752	0.867	<.0001				
Obesity								
(+) vs (-)	1.079	1.026	1.135	0.003				
Education								
High vs Low	0.895	0.854	0.939	<.0001				
Stress								
Heavy vs Light	1.225	1.161	1.293	<.0001				
Hypertension								
(+) vs (-)	0.779	0.69	0.88	<.0001				
Diabetes mellitus								
(+) vs (-)	1.309	1.204	1.424	<.0001				
Stroke								
(+) vs (-)	1.431	1.219	1.68	<.0001				
Bronchial Asthma								
(+) vs (-)	1.141	1.017	1.279	0.0243				
Allergic rhinitis								
(+) vs (-)	0.82	0.728	0.923	0.001	0.825	0.731	0.932	0.0019
Ca intake / day (100 unit)	1.016	1.009	1.023	<.0001				
Cholesterol	1.002	1.001	1.002	<.0001				
HbA1c	1.118	1.083	1.154	<.0001				

OR, odd ratio; CI, confidence interval; * Statistically significant ($p < 0.05$)

least 12 weeks in South Korea[12]. Because 25(OH)D is known to have anti-inflammatory properties leading to reduced inflammation[13-15], we hypothesized that low 25(OH)D level is related to the increased prevalence of CRS. Although previous studies have suggested an association between serum 25(OH)D level and prevalence of CRS[7-9], their results had some limitations by small sample sizes. Therefore, this study aimed to investigate the correlation between serum 25(OH)D level and CRS satisfying the diagnostic criteria of endoscopy-based CRS in adults using national health database from South Korea.

In contrast with previous studies, our results provided counter-evidence to prior works on the association of 25(OH)D levels and CRS showing a higher serum 25(OH)D level in the CRS group than in the control group. Furthermore, the clogit regression analysis showed the endoscopic finding of mucopurulent rhinorrhea showed higher ORs with a greater power of prediction for normal 25(OH)D. While prior research has suggested a link between low 25(OH)D levels and development of CRS, our study showed low serum 25(OH)D levels were not associated with increased prevalence of CRS in Korean adults. Our results could be used to advance a new opinion against previous findings regarding correlations between low 25(OH)D level and increased prevalence of CRS. Until now, several previous studies have shown that 25(OH)D deficiency is associated with increased risk of CRS in adults[7-9]. Pinto measured serum 25(OH)D levels in the clinical laboratory by using samples from urban African American and white adults with and without severe CRS and showed that serum 25(OH)D levels were significantly lower in urban African American subjects with CRS as compared with age- and sex-matched controls[7]. Furthermore, Wang showed that a significantly lower 25(OH)D level was found in a group of Taiwanese patients with CRS, revealing an association with greater nasal polyp size[9]. However, according to our results, endoscopy-based CRS was not an important predictor for low serum 25(OH)D level, in contrast with the previous study.

The discrepancy in results regarding the relationship between

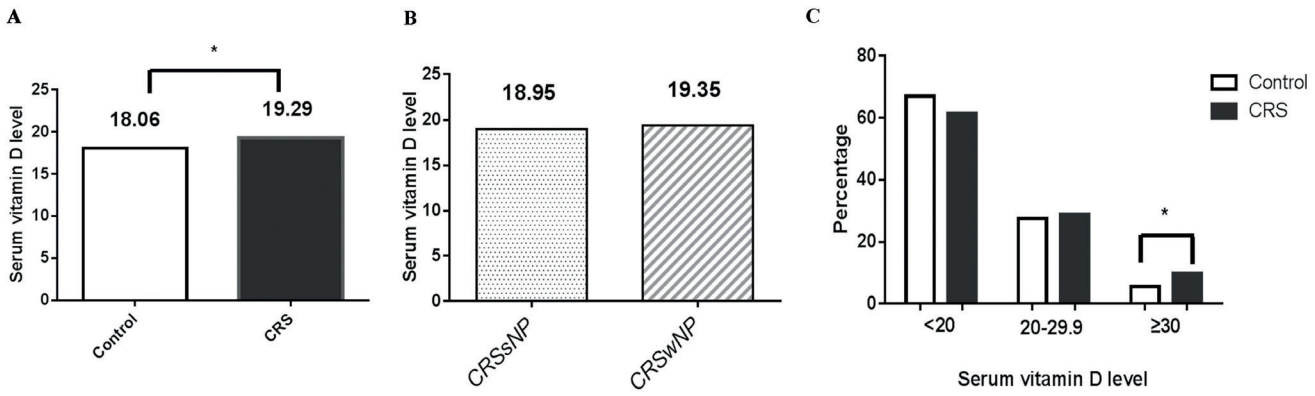

Figure 1. Comparison of 25(OH)D level between control and CRS groups. (a) As a continuous variable, the serum 25(OH)D level in the CRS group was significantly higher than that of the control group. (b) There was no statistical difference for 25(OH)D level between CRS with nasal polyp and CRS without nasal polyp. (c) As a categorical variable, the serum 25(OH)D level was significantly higher in the CRS group than in the control group only in the sufficient serum 25(OH)D group. The unit of 25(OH)D is ng/mL. CRS = chronic rhinosinusitis.

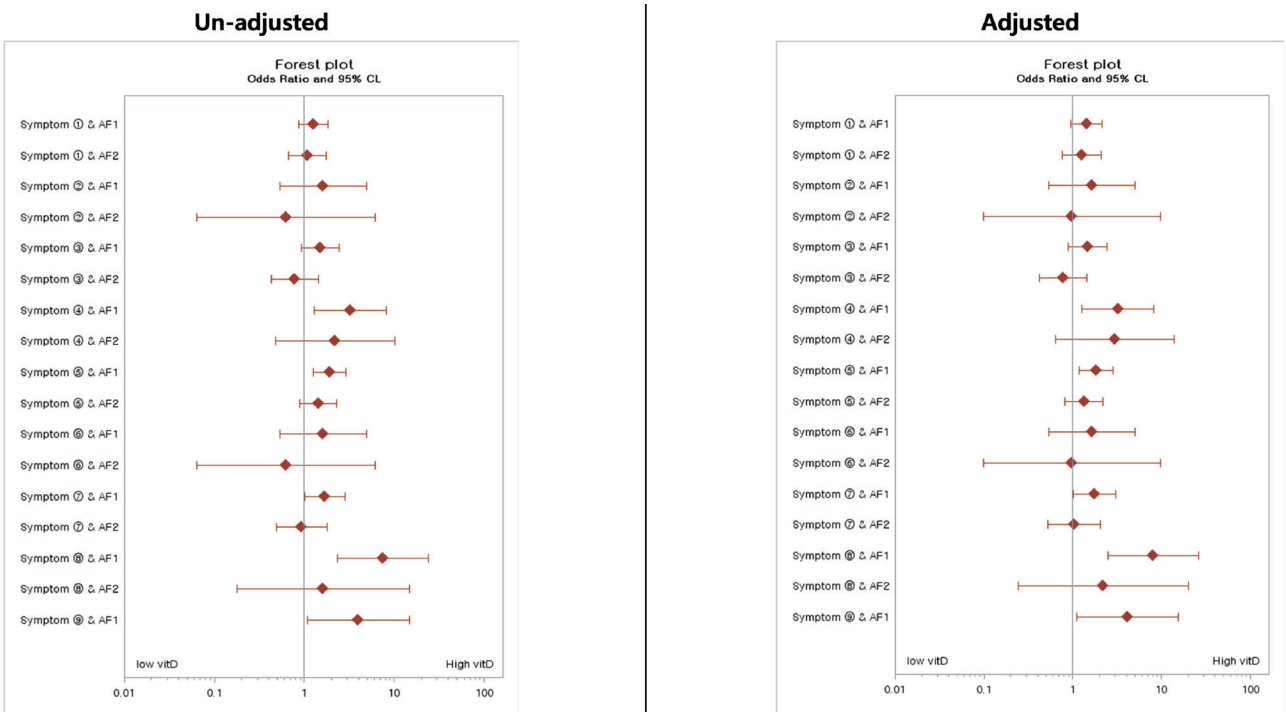

Figure 2. Relative importance of 25(OH)D level according to endoscopy-based CRS. The combinations including mucopurulent rhinorrhea at the middle meatus (AF1) showed generally higher serum 25(OH)D levels with high odds ratios. However, the combinations including nasal polyps on endoscopic exam (AF2) did not show significant odds ratios relevant to serum 25(OH)D level. S1, nasal obstruction and anterior/posterior nasal drip; S2, nasal obstruction and facial pain; S3, nasal obstruction and loss of smell; S4, anterior/posterior nasal drip and facial pain; S5, anterior/posterior nasal drip and loss of smell; S6, nasal obstruction, anterior/posterior nasal drip, and facial pain; S7, nasal obstruction, anterior/posterior nasal drip, and loss of smell; S8, anterior/posterior nasal drip, facial pain, and loss of smell; S9, nasal obstruction, anterior/posterior nasal drip, facial pain, and loss of smell; AF1, endoscopic finding of mucopurulent rhinorrhea at the middle meatus; AF2, endoscopic finding of nasal polyps.

serum 25(OH)D level and CRS might be explained as follows. First, the composition of the study population, including different races or sun exposure times, varies by country, resulting in different associations between serum 25(OH)D level and CRS prevalence. Second, while previous studies has some limitations by small sample sizes, our study includes a larger data set, which may help clarify the relationship between serum 25(OH)D level and CRS. Furthermore, unlike previous studies, this epidemiological study considered various demographic factors including sex, age, and allergic rhinitis which may affect serum 25(OH)

D levels. Third, the definition of CRS varied among studies; several guidelines and tools were used to diagnose CRS cohorts, whereas some studies made the diagnosis based on their own clinical and radiographic findings[7-9,16]. Also, previous studies included severe cases of CRS, which showed stage IV disease on computed tomographic analysis graded by the Harvard criteria[7]. The inclusion of only severe cases of CRS seems to have limited application for all cases of CRS, while the endoscopy-based CRS definition used in our study might be more reasonable because of the use of objective findings such as mucopurulent rhinorrhea or nasal polyp.

In this study, serum 25(OH)D level ranged from minimum of 1.98 ng/mL to maximum of 66.96 ng/mL, with mean serum 25(OH) D level of 18.065 (± 6.564) ng/mL and median value of 17.08 ng/mL. Cut-off values for extremely low serum 25(OH)D levels were measured according to existing literature[11]. Possibly, serum 25(OH)D level would have to be reduced to a highly significant level to result in clinically effective decrease in sinonasal immunity, as demonstrated by murine CRS animal models. Mulligan et al. showed that both 25(OH)D deficiency and *Aspergillus fumigatus* CRS mouse model were associated with altered sinonasal 25(OH)D metabolism, which caused reductions in local levels of active 25(OH)D metabolite even with adequate circulating 25(OH)D levels[17]. This experiment proved that the deficiency of circulating serum 25(OH)D level was not associated with CRS, which coincide with our results.

Recent findings on the function of 25(OH)D may explain aspects of the pathophysiology of various allergic diseases including allergic rhinitis and asthma[18,19]. Sultan et al. showed that sinonasal epithelial cells can generate active 25(OH)D, which can increase the expression of antimicrobial peptides such as cathelicidin[20]. This study suggests that 25(OH)D can act as an immune-modulating agent in host defense. Meanwhile, the role of 25(OH)D in the pathogenesis of inflammatory airway diseases such as chronic rhinosinusitis remains under investigation. Studies performed in Sao Paulo and Belgium could not reveal a relationship between sinusitis and chronic rhinitis[21,22]. Whereas, allergic rhinitis was considered as the most important risk factor of CRS in South Korea[23]. In other words, the Asiatic pathophysiology of CRS may differ from the European type, due to a synergism with allergic rhinitis[24]. Among demographic factors of this study, we found that female sex, low age, and allergic rhinitis were significant factors showing lower 25(OH) D levels. This result coincides with that of a previous study from South Korea on the association between lower serum 25(OH)D level and higher allergic rhinitis prevalence[25]. In regards to the association between allergic rhinitis and low serum 25(OH)D level, the conclusions from this epidemiologic study based on a large population made the opposite argument against previous work on the role of 25(OH)D in CRS, which was limited by a small number of shortcomings[7-9]. Systematic review showed that low serum 25(OH)D is more prevalent in patients with CRSwNP and in patients with eosinophilic or allergic fungal rhinosinusitis, although no definitive conclusion can be made on whether 25(OH)D is a causative factor in CRS[26]. We also identified some racial difference regarding the prevalence of 25(OH)D deficiency, and our results support that the Asiatic pathophysiology of CRS about serum 25(OH)D deficiency may differ from the European type. Therefore, this study reflected that the effect of serum 25(OH)D level on CRS can show different pathophysiology in South Korea, although the available evidence indicated a significant relationship between low 25(OH)D levels and CRS phenotypes.

Our study has some limitations. First, although the KNHANES is a large and complex survey, the sample size of CRS patients might be a limitation. The number of patients with CRS is quite small compared with controls. Second, this study is purely observational and epidemiological, like previous studies. Despite the nature of this study, CRS diagnosis was based on questionnaires about nasal symptoms along with positive endoscopic findings, such as mucopurulent rhinorrhea at the middle meatus or nasal polyp on endoscopy confirmed by otorhinolaryngology residents. As we chose objective diagnostic criteria of CRS using endoscopic findings compared to previous studies, the diagnostic criteria of endoscopy-based CRS could be considered more reasonable. Since there have been several arguments about this topic, further evidence of a causal or therapeutically-relevant linkage between 25(OH)D and CRS is required. Third, previous epidemiological studies have demonstrated ethnic and regional differences in 25(OH)D levels. In this study, the mean serum 25(OH)D level of individuals from South Korea was 19.48 ng/mL, whereas the mean serum 25(OH)D levels of individuals from the US and Canada are greater than 24 ng/mL[27-29]. Only 5.59% of participants showed serum 25(OH)D levels of 30 ng/mL or greater and this phenomenon may be influenced by indoor lifestyle and reduced light exposure time in South Korea. Because the skin pigmentation and national vitamin D food fortification programs are different according to nations, geographic and environmental effects on serum 25(OH)D level should be considered for future study.

Conclusion

In spite of some limitations, we found that the level of serum 25(OH)D level was higher in patients with CRS than without CRS from the 2008 to 2011 KNHANES in adults from South Korea. This means that serum 25(OH)D deficiency is not a possible risk factor in Korean adults with CRS contradicting those of previous studies. This study is the first epidemiological study to be conducted on the relationship between 25(OH)D and CRS, and it allows for meaningful questioning of previous findings of positive correlations between low 25(OH)D levels and CRS prevalence.

Authorship contribution

EJL: study concept and design; drafting of manuscript; manuscript revision. CSH: acquisition, analysis, and interpretation of data; approval of final version of manuscript to be published. K-SK: study concept and design; revision of manuscript; analysis and interpretation of data; approval of final version of manuscript to be published.

Conflict of interest

All authors declared no conflicts of interest.

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