Original Article
Cent Asian J Med Sci. 2022 March;8(1):14-23. https://doi.org/10.24079/CAJMS.2022.03.003

Central Asian Journal of Medical Sciences
CAJMS

Serum Vitamin E is Associated with Osteoarthritis among Korean Older Adults

Seonghee Park [1], Kyeong-Rae Kim [1], Hana Kwon [1], Kwang-Yeol Lee [2], Il-Tae Jang [3]

[1]Nanoori Medical Research Institute, Nanoori Hospital Gangnam, Seoul, Korea; [2]Department of Orthopedics, Nanoori Hospital Gangnam, Seoul, Korea; [3]Department of Neurosurgery, Nanoori Hospital Gangnam, Seoul, Korea

Submitted: January 20, 2022
Revised: January 28, 2022
Accepted: March 10, 2022

Corresponding Author
Il-Tae Jang , PhD
Department of Neurosurgery,
Nanoori Hospital Gangnam, Seoul
06048, Korea
Tel: +82-1688-9797
Fax: +82-2-6714-9103
E-mail: nanoori_research@naver.com

Objectives: We aimed to examine the cross-sectional association between serum vitamin E level and osteoarthritis in Korean older adults. **Methods:** Data from the Korea National Health and Nutrition Examination Survey 2016 – 2018 were used. Overall, 978 participants aged ≥ 65 years were included in the study. Demographic, lifestyle, and health data were obtained through interviews or self-reported questionnaires. Patients with osteoarthritis were defined if they had responded "yes" to any of these three questions related to diagnosis, current condition, and treatment. Multivariate logistic regression analysis was performed to assess the association between serum vitamin E level and osteoarthritis. **Results:** After multivariate adjustment, a higher level of vitamin E was found to be associated with a higher prevalence of osteoarthritis (Odds ratio: 2.27, 95 % Confidence Interval: 1.19 – 4.34, p for trend = 0.037). **Conclusion:** A higher level of serum vitamin E was associated with increased osteoarthritis prevalence in older Koreans. Further prospective or clinical studies are needed to verify the causality.

Keywords: Serum, Vitamin E, Osteoarthritis, Aged, Korea

Introduction

The world is facing changes in demographic structure as the of life expectancy increases, and the number of live births per woman decreases [1]. The United Nations reports that the world's population aged ≥ 65 years reached approximately 727 million in 2020 and will more than double to 1.5 billion by 2050 [1]. In South Korea, the number of persons aged ≥ 65 years is estimated to increase at the highest rate among other countries by 2050 [2]. In an emerging aging society, it is very important for elderly people to experience healthy aging, and thus, it is necessary to prevent and manage geriatric diseases [3].

Osteoarthritis, called degenerative arthritis, is one of the typical geriatric diseases [4]. About 33.1 million people worldwide have osteoarthritis [5]. In South Korea, 1,194,000 individuals in their 60s and 1,308,000 individuals aged ≥ 70 years received hospital treatment for osteoarthritis [6]. It has also been reported that osteoarthritis-related medical expenses per person increase with increasing age, and people in their 70s or older paid about KRW 530,000 for medical expenses related

to osteoarthritis [6]. Osteoarthritis is a disease in which in situ articular cartilage is destroyed and deformed, causing damage to bones and ligaments, and resulting in inflammation, pain, and dysfunction [4]. Osteoarthritis not only increases the burden of treatment costs for patients but also causes difficulties in the activities of daily living, which can deteriorate the quality of life [7]. In addition, the risk of its complications, such as cardiovascular disease, metabolic syndrome, depression, and associated mortality, may increase [8].

Various factors affect an individuals' joint health [9, 10]. Vitamin E, a fat-soluble vitamin with antioxidant activity [10, 11], is known to have positive effects on osteoarthritis caused by articular cartilage damage by oxygen species, which are excessively generated due to oxidative stress in the body [12]. Several epidemiological studies have evaluated the association between vitamin E and osteoarthritis. A study involving patients with osteoarthritis aged 50 – 70 years old in northern India found that the levels of serum inflammatory markers, such as plasma C - reactive protein and interleukin 6, were significantly lower in those receiving vitamin E supplementation compared to those in control group [13]. A study with 35 osteoarthritis patients showed a negative association between serum vitamin E levels and osteoarthritis pain scores [14]. The Swedish National March Cohort study found that the risk of osteoarthritis increased with higher dietary vitamin E intake level [15]. A cross-sectional study conducted in Changsha City, Hunan, China, found no significant association between dietary vitamin E and the prevalence of osteoarthritis [16]. These studies showed inconsistent results regarding the association between vitamin E and osteoarthritis. Furthermore, some of these studies were not fully consider the confounding factors or have insufficient sample size. Above all, to the best our knowledge, no studies have been conducted the association between serum vitamin E and osteoarthritis in Korean elderly so far. Considering that elderly population in South Korea is gradually increasing as the aging is rapidly progressing, community-based epidemiological studies are needed to evaluate this association.

Therefore, this study aimed to determine the association between serum vitamin E levels and osteoarthritis in Korean older adults aged ≥ 65 years using data from the Korea National Health and Nutrition Examination Survey (KNHANES).

Materials and Methods

Study population

The KNHANES is a large-scale nationwide representative cross-sectional study [17]. It is conducted to produce national statistics through a survey of health and nutritional status and health-related awareness and behavior of the Korean population [17]. The KNHANES was first started in 1998, and has been regularly

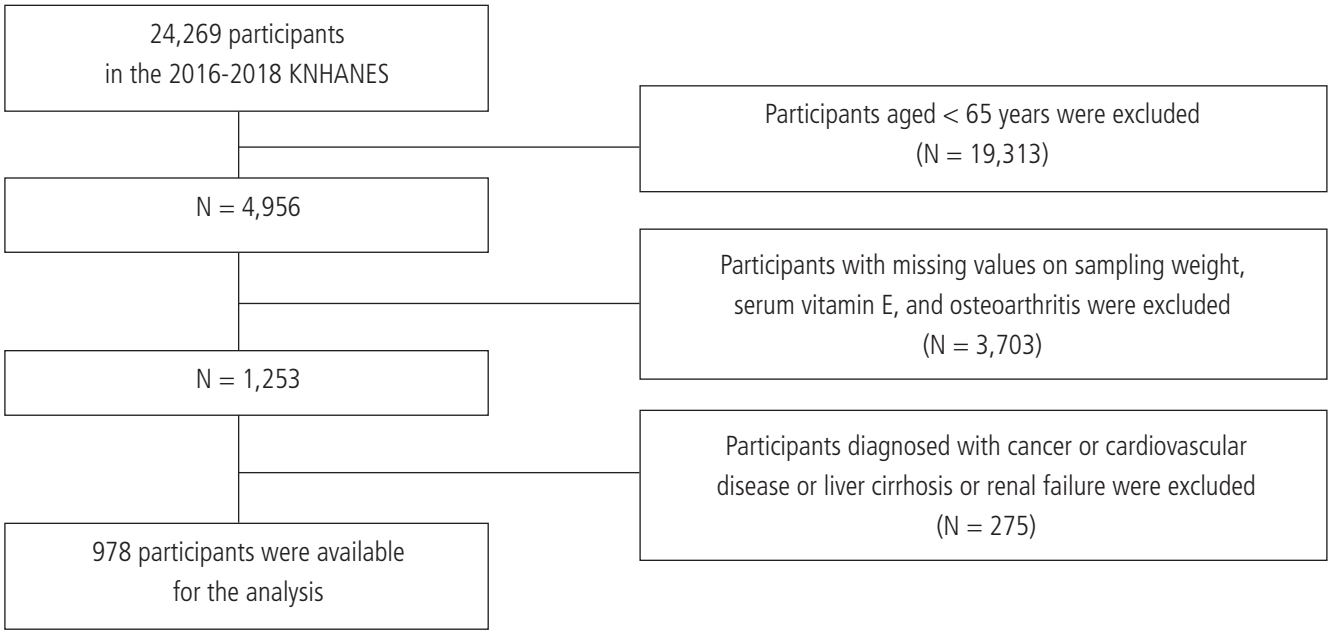

Figure 1. Flow chart of participants: Korea National Health and Nutrition Examination Survey (KNHANES) 2016-2018.

conducted thereafter. Initially, it was conducted every 3 – 4 years (1998, 2001, and 2005); since 2007, an annual survey using a rolling sampling system has been conducted to avoid seasonal bias. The 8th KNHANES (2019 – 2021) is currently being conducted [18]. Details of the data collection and survey protocols have been described in a previous study [17].

In this study, we analyzed data from 2016 to 2018, during which serum vitamin E level was assessed. Of the 24,269 participants, those aged < 65 years (n = 19,313), those with missing values for sampling weight or serum vitamin E or osteoarthritis (n = 3,703), those diagnosed with cancer or cardiovascular disease or liver cirrhosis or renal failure at the time of the survey (n = 275) were excluded. Ultimately, 978 participants were included in the analysis (Figure 1).

Demographic and lifestyle information

Data on participants' demographic information such as age, sex, education level, and household income were obtained through interviews conducted by trained investigators, while data on health behavior such as physical activity level, alcohol consumption, and smoking status were collected through self-reported questionnaires. Education level was categorized into "elementary school or lower", "middle school graduate", "high school graduate", and "college graduate or higher". Household income was divided into quartiles according to the monthly average equalized income – low, mid-low, mid-high, and high. Concerning physical activity level, metabolic equivalent tasks (METs - h/week) were calculated by multiplying the number of days and hours for each type of physical activity (walking/moderate intensity/high intensity) and weights assigned to each intensity level [19]; these were categorized into tertiles. Alcohol consumption was classified as "drinkers" and "non-drinkers" based on the consumed alcohol within the past year, and smoking status was also divided into "current smokers" and "non-smokers". Regarding dietary supplement use, the participants had answered a question, "Use of a dietary supplement for ≥ 2 weeks in the past year", and categorized as "users" and "non-users" based on their response.

Anthropometry and blood information

Anthropometric measurement and blood sample collection were conducted by trained staff in accordance with the "KNHANES Health Examination Guidelines" [20].

Body weight and height were measured using a standardized height and weight scale. Participants were guided by investigators to stand in an upright position after removing their clothes and socks, and wearing examination gown. Body mass index (BMI) was calculated by dividing weight (kg) by the square of the height (m^2). The World Health Organization criteria for Asian populations were used to identify participants with underweight/normal weight (BMI < 23 kg/m^2), overweight (23 ≤ BMI < 25 kg/m^2), and obesity (BMI ≥25 kg/m^2) [21].

Blood samples were collected after at least 8 h of fasting [20]. Participants were excluded from blood draws if they were hemophiliacs or took an anticoagulants or had a chemotherapy within a month [20]. Individuals aged ≥ 80 years or had rashes on both arms or open wounds or vascular problems were also excluded [20]. Blood was drawn from the median cubital vein or cephalic vein of the nondominant arm [20]. Serum vitamin E level was measured at Seegene Medical Foundation using high-performance liquid chromatography-UV detection (Agilent Technologies, Inc., Santa Clara, CA, USA) [22].

Definition of osteoarthritis

Osteoarthritis was defined using the questions as follows; "Have you ever been diagnosed with osteoarthritis by a doctor?" "Are you currently experiencing osteoarthritis?" "Are you receiving treatment for osteoarthritis?" Individuals who responded "yes" to any questions related to diagnosis, current condition, and treatment were included in the osteoarthritis group.

Statistical analysis

To integrate the KNHANES data (2016–2018), a complex sample design and all related parameters–primary sampling units, stratification variables, and statistical weights were considered in the analysis. A detailed description of the sampling method, stratification, and weight have been provided in a previous study [17].

The χ^2 test or one-way analysis of variance (ANOVA) test or t-test was used to compare the general characteristics between groups. Categorical and continuous variables were presented as frequencies and percentages and as means and standard deviations, respectively. For ANOVA test, differences in the means between quintiles of serum vitamin E levels were tested using Tukey's test. Multivariate logistic regression analysis was performed to examine the association between serum vitamin E

levels and osteoarthritis and calculate the odds ratio (OR) and 95 % confidence interval (CI). Potential confounding factors were considered through a literature review [23, 24] and preliminary analysis and selected risk factors associated with osteoarthritis or variables associated with serum vitamin E levels. Potential effect modification was examined using multiplicative terms of the statistical model, and no significant effect modifier was observed. To systematically account for potential confounding factors, three covariate models were evaluated. Model 1 was unadjusted; Model 2 was adjusted for age, sex, household income, education level, smoking status, alcohol consumption, physical activity level, body mass index, and type 2 diabetes; Model 3 was adjusted for all variables included in Model 2 as well as dietary supplement use and total energy intake. P for trend was calculated using the median value of quintiles.

All statistical analyses were performed using the Statistical Analysis System version 9.4 (SAS Institute, Cary, NC, USA), and statistical significance was tested in $\alpha < 0.05$.

Ethical statement

The study was performed by the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All data in this study were collected after obtaining written consent from each participant. Data collection and analysis for this study were approved by the Institutional Review Boards (IRBs) of the Korea Disease Control and Prevention Agency (approval number: 2018-01-03-P-A) [25]. Additionally, this study was granted exemption from deliberation by the IRB of affiliated institution (approval number: NR-IRB 2021-012).

Results

General characteristics of participants according to serum vitamin E levels

The general characteristics of the participants according to serum vitamin E levels are shown in Table 1. The median of serum vitamin E levels for quintiles 1, 2, 3, 4, and 5 were 8.91, 11.31, 13.34, 15.59, and 20.42, respectively; the average age was 73.31, 72.86, 72.66, 71.36, and 71.90 years, respectively, and the proportion of women was 41.54 %, 48.98 %, 54.87 %, 64.14 %, and 63.92 %, respectively. The proportion of participants with a high household income and dietary supplement use ranged from 21.94 % to 34.85 % and from 38.29 % to 68.57 % across quintiles of serum vitamin E levels, respectively. The proportion of current smokers was 16.49 %, 5.64 %, 9.84 %, 9.28 %, and 8.81 % in quintiles 1, 2, 3, 4, and 5, respectively.

General characteristics of participants according to osteoarthritis status

Table 2 presents the general characteristics according to osteoarthritis status. Of the 978 participants, 707 participants were included in the non-osteoarthritis group and 271 participants were included in the osteoarthritis group. The osteoarthritis group had a higher proportion of women than the non-osteoarthritis group (83.03 % vs. 43.85 %). Approximately 34.01 % in non-osteoarthritis group graduated high school or higher, while only 16.85 % patients with osteoarthritis graduated high school or higher. The proportion of participants who had a higher physical activity level was 35.99 % and 25.93 % in non-osteoarthritis group and osteoarthritis group, respectively. The proportion of participants whose BMI ≥ 25 kg/m^2 was 34.00 % and 48.15 % in non-osteoarthritis group and osteoarthritis group, respectively. The proportion of drinkers was 57.26 % and 43.45 %, and the proportion of current smokers was 11.98 % and 4.85 %, in non-osteoarthritis group and osteoarthritis group, respectively.

Association between serum vitamin E levels and osteoarthritis

The association between serum vitamin E levels and osteoarthritis is shown in Table 3. In the crude model (Model 1), the highest quintile of serum vitamin E levels showed a significantly higher prevalence of osteoarthritis compare to the lowest quintile (OR: 2.48, 95 % CI: 1.43–4.30, p for trend = 0.004). This association remained significant in Model 2 and fully adjusted Model 3 (Model 2, OR: 2.21, 95 % CI: 1.16 – 4.21, p for trend = 0.043, and Model 3, OR: 2.27, 95 % CI: 1.19 – 4.34, p for trend = 0.037).

Table 1. General characteristics of participants according to serum vitamin E levels.

Characteristics	Serum vitamin E levels (mg/L)					p-value [1]
	Q1	Q2	Q3	Q4	Q5	
	195	196	195	198	194	
Serum vitamin E, range (median)	3.68–10.22 (8.91)	10.24–12.24 (11.31)	12.25–14.41 (13.34)	14.43–17.20 (15.59)	17.21–57.12 (20.42)	
Age (years) [2]	73.31 ± 5.10	72.86 ± 5.00	72.66 ± 5.18	71.36 ± 5.03	71.90 ± 4.78	0.001
Sex						
Men	114 (58.46)	100 (51.02)	88 (45.13)	71 (35.86)	70 (36.08)	0.001
Women	81 (41.54)	96 (48.98)	107 (54.87)	127 (64.14)	124 (63.92)	
Education level						
Elementary school or lower	104 (55.91)	111 (56.92)	108 (56.25)	112 (56.57)	106 (54.92)	0.646
Middle school graduate	25 (13.44)	30 (15.38)	33 (17.19)	26 (13.13)	27 (13.99)	
High school graduate	42 (22.58)	33 (16.92)	34 (17.71)	31 (15.66)	40 (20.73)	
College graduate or higher	15 (8.06)	21 (10.77)	17 (8.85)	29 (14.65)	20 (10.36)	
Household income						
Low	62 (32.29)	57 (29.08)	39 (20.21)	43 (21.72)	34 (17.62)	0.008
Mid-low	35 (18.23)	50 (25.51)	51 (26.42)	38 (19.19)	44 (22.80)	
Mid-high	50 (26.04)	46 (23.47)	53 (27.46)	48 (24.24)	57 (29.53)	
High	45 (23.44)	43 (21.94)	50 (25.91)	69 (34.85)	58 (30.05)	
Physical activity level [3]						
Low	68 (35.60)	69 (35.20)	71 (36.60)	72 (36.36)	65 (33.51)	0.997
Mid	60 (31.41)	65 (33.16)	57 (29.38)	60 (30.30)	63 (32.47)	
High	63 (32.98)	62 (31.63)	66 (34.02)	66 (33.33)	66 (34.02)	
Body mass index (kg/m ^{2})						
< 23	83 (43.01)	63 (32.47)	81 (41.75)	63 (31.82)	65 (33.51)	0.084
23 – 25	37 (19.17)	53 (27.32)	43 (22.16)	62 (31.31)	54 (27.84)	
≥ 25	73 (37.82)	78 (40.21)	70 (36.08)	73 (36.87)	75 (38.66)	
Dietary supplement						
Non-users	108 (61.71)	98 (55.68)	94 (54.02)	76 (41.76)	55 (31.43)	0.001
Users	67 (38.29)	78 (44.32)	80 (45.98)	106 (58.24)	120 (68.57)	
Alcohol consumption						
Non-drinkers	88 (45.60)	104 (53.33)	82 (42.27)	88 (45.13)	89 (46.35)	0.261
Drinkers	105 (54.40)	91 (46.67)	112 (57.73)	107 (54.87)	103 (53.65)	
Smoking status						
Non-smokers	162 (83.51)	184 (94.36)	174 (90.16)	176 (90.72)	176 (91.19)	0.009
Current smokers	32 (16.49)	11 (5.64)	19 (9.84)	18 (9.28)	17 (8.81)	

Q, quintile; Values are expressed as the mean ± standard deviation or n (%); [1] p values were derived from χ^2 test for categorical variables and one-way analysis of variance test for continuous variables; [2] As a result of Tukey's multiple comparison test, Q1 and Q4, Q1 and Q5, Q2 and Q4 has a significant difference in age between serum vitamin E groups; [3] The physical activity level was calculated in terms of metabolic equivalent tasks (METs-h/week) and categorized into tertiles.

Table 2. General characteristics of participants according to osteoarthritis status.

Characteristics	Total	Non-osteoarthritis	Osteoarthritis	p-value [1]
	978	707	271	
Serum vitamin E, range (median)	3.68–57.12 (13.35)	4.25–45.07 (13.09)	3.68–57.12 (13.65)	
Age (years)	72.42 ± 5.06	72.24 ± 5.10	72.86 ± 4.91	0.087
Sex				
Men	443 (45.30)	397 (56.15)	46 (16.97)	0.001
Women	535 (54.70)	310 (43.85)	225 (83.03)	
Education level				
Elementary school or lower	541 (56.12)	357 (51.22)	184 (68.91)	0.001
Middle school graduate	141 (14.63)	103 (14.78)	38 (14.23)	
High school graduate	180 (18.67)	146 (20.95)	34 (12.73)	
College graduate or higher	102 (10.58)	91 (13.06)	11 (4.12)	
Household income				
Low	235 (24.18)	176 (25.04)	59 (21.93)	0.464
Mid-low	218 (22.43)	149 (21.19)	69 (25.65)	
Mid-high	254 (26.13)	185 (26.32)	69 (25.65)	
High	265 (27.26)	193 (27.45)	72 (26.77)	
Physical activity level [2]				
Low	345 (35.46)	233 (33.14)	112 (41.48)	0.007
Mid	305 (31.35)	217 (30.87)	88 (32.59)	
High	323 (33.20)	253 (35.99)	70 (25.93)	
Body mass index (kg/m^2)				
< 23	355 (36.49)	286 (40.68)	69 (25.56)	0.001
23 – 25	249 (25.59)	178 (25.32)	71 (26.30)	
≥ 25	369 (37.92)	239 (34.00)	130 (48.15)	
Dietary supplement				
Non-users	431 (48.87)	327 (51.01)	104 (43.15)	0.037
Users	451 (51.13)	314 (48.99)	137 (56.85)	
Alcohol consumption				
Non-drinkers	451 (46.54)	300 (42.74)	151 (56.55)	0.001
Drinkers	518 (53.46)	402 (57.26)	116 (43.45)	
Smoking status				
Non-smokers	872 (89.99)	617 (88.02)	255 (95.15)	0.001
Current smokers	97 (10.01)	84 (11.98)	13 (4.85)	

Values are expressed as the mean ± standard deviation or n (%); [1]p-values were derived from χ^2 test for categorical variables and t-test for continuous variables; [2] The physical activity level was calculated in terms of metabolic equivalent tasks (METs-h/week) and categorized into tertials.

Table 3. Odds ratios and 95 % confidence intervals for osteoarthritis.

Characteristics	Model 1		Model 2		Model 3	
	OR (95 % CI)	p-value	OR (95 % CI)	p-value	OR (95 % CI)	p-value
			1.02 (0.97-1.06)	0.487	1.01 (0.97–1.06)	0.604
Sex						
Men			Reference			
Women			3.69 (2.16–6.29)	0.001	3.42 (1.99–5.87)	0.001
Education level						
Elementary school or lower			Reference			
Middle school graduate			0.73 (0.42–1.28)	0.273	0.72 (0.41–1.26)	0.247
High school graduate			0.68 (0.37–1.26)	0.217	0.70 (0.38–1.29)	0.251
College graduate or higher			0.49 (0.20–1.20)	0.117	0.50 (0.20–1.23)	0.129
Household income						
Low			Reference			
Mid-low			1.54 (0.87–2.73)	0.138	1.55 (0.88–2.75)	0.129
Mid-high			1.08 (0.60–1.95)	0.799	1.09 (0.61–1.97)	0.766
High			1.21 (0.67–2.18)	0.521	1.25 (0.69–2.26)	0.458
Physical activity level [2]						
Low			Reference			
Mid			0.76 (0.45–1.29)	0.314	0.77 (0.45–1.29)	0.317
High			0.72 (0.44–1.17)	0.179	0.72 (0.44–1.18)	0.191
Body mass index (kg/m^2)						
< 23			Reference			
23 – 25			2.38 (1.33–4.26)	0.004	2.35 (1.32–4.21)	0.004
≥ 25			3.01 (1.85–4.89)	0.001	3.05 (1.87–4.99)	0.001
Alcohol consumption						
Non-drinkers			Reference			
Drinkers			0.81 (0.52–1.27)	0.365	0.82 (0.53–1.29)	0.394
Smoking status						
Non-smokers			Reference			
Current smokers			0.81 (0.34–1.92)	0.631	0.81 (0.34–1.92)	0.631
Type 2 diabetes						
No			Reference			
Yes			1.20 (0.74–1.95)	0.460	1.18 (0.72–1.92)	0.509
Dietary supplement						
Non-users			Reference			
Users					1.31 (0.83–2.05)	0.246
Total energy intake (g)					1.00 (0.99–1.00)	0.281
Serum vitamin E levels (mg/L)						
Q1			Reference			
Q2	1.27 (0.71–2.27)	0.414	1.22 (0.62–2.39)	0.565	1.26 (0.64–2.48)	0.504
Q3	1.74 (0.97–3.12)	0.065	1.58 (0.78–3.19)	0.203	1.58 (0.79–3.18)	0.199
Q4	1.02 (0.59–1.76)	0.935	0.82 (0.41–1.64)	0.568	0.84 (0.42–1.67)	0.607
Q5	2.48 (1.43–4.30)	0.001	2.21 (1.16–4.21)	0.017	2.27 (1.19–4.34)	0.013
p for trend[1]	0.004		0.043		0.037	

OR, odds ratio; CI, confidence interval; Q, quintile; [1]p for trend was evaluated by assigning the median values of each quintile of serum level to a continuous variable; Model 1: unadjusted; Model 2: adjusted age, sex, household income, education level, smoking status, alcohol consumption, physical activity level, body mass index, and type 2 diabetes; Model 3: additionally adjusted for dietary supplement use and total energy intake.

Discussion

This study investigated the association between serum vitamin E levels and osteoarthritis in older adults aged ≥ 65 years using data from the KNHANES 2016 – 2018. The prevalence of osteoarthritis was significantly higher in those with the highest serum vitamin E levels than their counterparts, and this association was linear.

Vitamin E is a generic term for four tocopherols and four tocotrienols commonly found in food [26], of which alpha-tocopherol is known to be the dominant form in our body [26]. Although vitamin E is responsible for several functions in the body [27], it has been reported that vitamin E has positive effects on osteoarthritis, typically through its antioxidant and anti-inflammatory activities [11, 28]. Oxidative stress represents a state of imbalance of oxidants and antioxidants in the body, and the excessive accumulation of oxidants can cause inflammatory responses [29]. Osteoarthritis is also a disease that is caused by such inflammatory responses and may occur when accumulated oxidants activate the NF-kB pathway, resulting in chondrocyte aging and apoptosis [12]. However, when vitamin E is present in the body, active oxygen, that is, peroxyl radicals, reacts with alpha-tocopherol instead of lipid hydroperoxide, thereby stopping chain reactions of peroxyl radical formation [11].

In the present study, however, the prevalence of osteoarthritis was significantly higher as the serum vitamin E levels increase. This is consistent with the results of some previous studies. A nested case-control study using data from the Multicentre Osteoarthritis Study examined the association of baseline levels of serum vitamin E (alpha-tocopherol only) with incident whole knee radiographic osteoarthritis. After 30 months follow-up of the participants average aged 61 years, the incident of osteoarthritis was 1.89 times higher in those with the highest serum vitamin E levels compared to those with the lowest serum vitamin E levels (OR: 1.89, 95 % CI: 1.02–3.50, p for trend = 0.030) [30]. A prospective study using Swedish National March Cohort followed over 40 years' middle-aged adults for up to 19 years to examine the association between dietary intake of vitamin E and osteoarthritis. As the result, the participant's mean age was 58 years, and a positive linear association was shown between dietary intake of vitamin E and risk of osteoarthritis (hazard ratio [HR]: 1.11, 95 % CI: 1.02 – 1.21, p for trend = 0.01) [15]. Vitamin E can act as a harmful prooxidant in high concentrations [31, 32]. When excess alpha-tocopherol reacts with free radicals, it becomes a radical itself. If there is insufficient levels of ascorbic acid required for regeneration, alpha-tocopherol remains in a highly reactive state, ultimately promoting fatty acid and cellular oxidation in the body [31, 32]. The mechanisms that clearly explain the association between high serum vitamin E levels and osteoarthritis are limited. Therefore, further studies for the causal relationship and related mechanisms between vitamin E and osteoarthritis should be investigated.

This study has several limitations. First, as the KNHANES is a cross-sectional study and information of participants was collected at one point in time, the causal relationship between serum vitamin E levels and osteoarthritis could not be clarified. Second, osteoarthritis was evaluated using a binary-format self-reported questionnaire. Therefore, there is a possibility of potential diagnostic errors, and details such as the severity of the disease or the scope of symptoms cannot be considered. Third, limited information on dietary supplement in KNHANES; hence, the intake of vitamin E through dietary supplement could not be considered. Finally, although we adjusted for potential confounders through a literature review and a preliminary analysis, there might be influences of residual confounding factors that were not measured or were unknown. The causal relationship between serum vitamin E and osteoarthritis should be investigated in a subsequent large-scale prospective cohort study that considers detailed osteoarthritis diagnostic data with minimum measurement errors as well as dietary vitamin E supplement intake.

Despite these limitations, to the best our knowledge, this is the first study to investigate the association between serum vitamin E levels and osteoarthritis in elderly Korean people. We hope that the findings of this study will provide basic scientific data for the prevention and management of osteoarthritis in older people.

Conclusion

There was a significant positive linear association between serum vitamin E levels and the prevalence of osteoarthritis in older Koreans. Therefore, it is considered necessary to maintain appropriate vitamin E levels in the body for the prevention of osteoarthritis in people aged ≥ 65 years.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgements

KNHANES is an ongoing survey that assess the health and nutritional status of residents of the Republic of Korea, and provides data for the development and evaluation of national health policies and programs. The authors are thankful to investigators and participants of KNHANES 2016–2018.

Author contribution

Conceptualization, K.-R.K., H.N.K. and S.P.; Validation, K.Y.L. and I.-T.J.; Methodology, K.-R.K., H.N.K. and S.P.; Software, Data Curation, Formal analysis, Visualization, and Writing—original draft Preparation, S.P.; Writing—Review and Editing, K.Y.L. and I.-T.J.; Supervision, I.-T.J. All authors have read and agreed to the published version of the manuscript.

Funding

This research did not receive any specific grant funding from agencies in the public commercial, or not for profit sectors.

References

1. United Nations. World population ageing 2020 [accessed on 20 October 2021]. Available at: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/undesa_pd-2020_world_population_ageing_highlights.pdf.
2. United Nations. World population ageing 2019 [accessed on 20 October 2021]. Available at: https://www.un.org/en/development/desa/population/publications/pdf/ageing/World Population Ageing 2019-Report.pdf.
3. Duplaga M, Grysztar M, Rodzinka M, Kopec A. Scoping review of health promotion and disease prevention interventions addressed to elderly people. BMC Health Serv Res 2016;16 Suppl 5: 278.
4. The Korean Orthopaedic Association. Osteoarthritis [accessed on 20 October 2021]. Available at: https://www.koa.or.kr/file/ %EA %B3 %A8 %EA %B4 %80 %EC %A0 %88 %EC %97 %BC_ %EC %95 %88 %EB %82 %B4_ %EC %B1 %85 %EC %9E %90.pdf.
5. Safiri S, Kolahi AA, Smith E, Hill C, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. Ann Rheum Dis 2020; 79: 819-28.
6. Health Insurance Review & Assessment Service. Healthcare big data analysis-family month special [accessed on 15 September 2021]. Available at: https://www.mohw.go.kr/react/al/sal0301vw.jsp?PAR_MENU_ID = 04&MENU_ID = 0403&page = 12&CONT_SEQ = 349360&SEARCHKEY = TITLE.
7. Centers for Disease Control and Prevention. A national public health agenda for osteoarthritis 2020 [accessed on 15 September 2021]. Available at: https://www.cdc.gov/arthritis/docs/oaagenda2020.pdf.
8. Swain S, Sarmanova A, Coupland C, Doherty M, Zhang W. Comorbidities in osteoarthritis: a systematic review and meta-analysis of observational studies. Arthritis Care Res (Hoboken) 2020; 72: 991-1000.
9. Abramoff B, Caldera FE. Osteoarthritis: pathology, diagnosis, and treatment options. Med Clin North Am 2020; 104: 293-311.
10. Odkhuu E, Narmandakh S, Zinamyadar M, Bold J, Amgalanbaatar A, Sundui E. Vitamin regulation of osteoclast differentiation. Cent Asian J Med Sci 2020; 6: 114-28.
11. Lee GY, Han SN. The role of vitamin E in immunity. Nutrients 2018; 10: 1614. doi: 10.3390/nu10111614.
12. Chin KY, Ima-Nirwana S. The role of vitamin E in preventing and treating osteoarthritis - a review of the current evidence. Front Pharmacol 2018; 9: 946-9.
13. Bhattacharya I, Saxena R, Gupta V. Efficacy of vitamin E in knee osteoarthritis management of North Indian geriatric population. Ther Adv Musculoskelet Dis 2012; 4: 11-9.
14. Eftekharsadat B, Aghamohammadi D, Dolatkhah N, Hashemian M, Salami H. Lower serum levels of alpha tocopherol and lycopene are associated with higher pain and physical disability in subjects with primary knee osteoarthritis: a case-control study. Int J Vitam Nutr Res 2021; 91: 304-14.
15. Veen L, Hantikainen E, Bellocco R, Ye W, Serafini M, Ponzano

M, et al. Dietary antioxidants, non-enzymatic antioxidant capacity and the risk of osteoarthritis in the Swedish National March Cohort. Eur J Nutr 2021; 60: 169-78.

16. Li H, Zeng C, Wei J, Yang T, Gao SG, Li YS, et al. Associations between dietary antioxidants intake and radiographic knee osteoarthritis. Clin Rheumatol 2016; 35: 1585-92.
17. Kweon SH, Kim YA, Jang MJ, Kim YJ, Kim KR, Choi SH, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014; 43: 69-77.
18. Korea Disease Control and Prevention Agency. Implementation state of Korea National Health and Nutrition Examination Survey [accessed on 2 September 2021]. Available at: https://knhanes.kdca.go.kr/knhanes/sub01/sub01_02.do.
19. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993; 25: 71-80.
20. Korea Disease Control and Prevention Agency. Guidelines for examination and inspection [accessed on 31 October 2021]. Available at: https://knhanes.cdc.go.kr/knhanes/sub04/sub04_02_02.do?classType = 4.
21. World Health Organization. The Asia-Pacific perspective: redefining obesity and its treatment [accessed on 31 October 2021]. Available at: https://apps.who.int/iris/bitstream/handle/10665/206936/0957708211_eng.pdf?sequence = 1&isAllowed = y.
22. Song SH. Quality control of the clinical laboratory for the Korea National Health and Nutrition Examination Survey (KNHANES) (2018, 7th third year) [accessed on 2 November 2021]. Available at: https://www.prism.go.kr/homepage/entire/researchDetail.do.
23. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. Best Pract Res Clin Rheumatol 2014; 28: 5-15.
24. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. Curr Opin Rheumatol 2018; 30: 160-7.
25. Korea Disease Control and Prevention Agency. Guidelines for the use of raw data for Korea National Health and Nutrition Examination Survey [accessed on 2 September 2021]. Available at: https://knhanes.kdca.go.kr/knhanes/sub03/sub03_06_02.do.
26. Jiang Q. Natural forms of vitamin E: metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. Free Radic Biol Med 2014; 72: 76-90.
27. Rizvi S, Raza ST, Ahmed F, Ahmad A, Abbas S, Mahdi F. The role of vitamin E in human health and some diseases. Sultan Qaboos Univ Med J 2014; 14: e157-65.
28. Wallert M, Börmel L, Lorkowski S. Inflammatory diseases and Vitamin E-what do we know and where do we go? Mol Nutr Food Res 2021; 65: e2000097.
29. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. Oxidative stress, aging, and diseases. Clin Interv Aging 2018; 13: 757-72.
30. Chaganti RK, Tolstykh I, Javaid MK, Neogi T, Torner J, Curtis J, et al. High plasma levels of vitamin C and E are associated with incident radiographic knee osteoarthritis. Osteoarthritis Cartilage 2014; 22: 190-6.
31. Sotler R, Poljšak B, Dahmane R, Jukić T, Pavan Jukić D, Rotim C, et al. Prooxidant activities of antioxidants and their impact on health. Acta Clin Croat 2019; 58: 726-36.
32. Carocho M, Ferreira IC. A review on antioxidants, prooxidants and related controversy: natural and synthetic compounds, screening and analysis methodologies and future perspectives. Food Chem Toxicol 2013; 51:15-25.