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Vitamin D status and associated metabolic risk factors among North Korean refugees in South Korea: a cross-sectional study

Kyeong Jin Kim,1 Yoon Jung Kim,2 Sun Hwa Kim,1 Jee Hyun An,1 Hye Jin Yoo,1 Hee Young Kim,1 Ji A Seo,1 Sin Gon Kim,1 Nan Hee Kim,1 Kyung Mook Choi,1 Sei Hyun Baik,1 Dong Seop Choi,1 Nam Hoon Kim1

ABSTRACT

Objective: Vitamin D deficiency is now recognised as a common health problem associated with various chronic diseases; however, it has not been fully elucidated among the minority groups. Here, we aimed to investigate the prevalence of vitamin D deficiency and its associated metabolic risk factors among North Korean refugees living in South Korea.

Design: Cross-sectional analysis from the longitudinal cohort, the North Korean refugee health in South Korea (NORNS) study.

Participants: A total of 386 North Korean refugees aged ≥30 years, who measured serum 25-hydroxy vitamin D (25(OH)D) level.

Results: The prevalence of vitamin D deficiency (25(OH)D <20 ng/mL) was 87% and no participants had an adequate vitamin D level (25(OH)D ≥30 ng/mL). Underweight participants (body mass index (BMI) <18 kg/m²) had significantly lower 25(OH)D levels than individuals with normal BMI (≥18.5 and <23 kg/m²). In the multivariate logistic regression analysis, the lowest 25(OH)D level (<10 ng/mL) was significantly associated with metabolic syndrome (OR, 6.37, 95% CI 1.34 to 30.3), high triglyceride (OR, 6.71, 95% CI 1.75 to 25.7), and high low-density lipoprotein (OR, 5.98, 95% CI 1.54 to 23.2) compared with 25(OH)D levels ≥20 ng/mL after adjusting for age, sex, season, length of residence in South Korea, physical activity and BMI.

Conclusions: Vitamin D deficiency is very common among North Korean refugees in South Korea. Despite their lower BMI, vitamin D deficiency was associated with metabolic syndrome in this population.

INTRODUCTION

Vitamin D deficiency, which is defined as a serum 25-hydroxy vitamin D (25(OH)D) level of less than 20 ng/mL, has been a common health problem in modern society.1 Traditionally, vitamin D serves as an important factor for bone health and mineral metabolism.2 Recent growing evidence indicates that a low vitamin D status is also closely associated with a variety of non-skeletal health problems, including infection, autoimmune disease, obesity and cardiometabolic diseases.3–4 Several large epidemiological studies showed that the prevalence of vitamin D deficiency or insufficiency was high, ranging between 25% and 64%.5–7 In South Korea, the prevalence of vitamin D deficiency is also high. According to the Fourth Korea National Health and Nutrition Examination Survey (KNHANES IV) from 2008, the prevalence of a low vitamin D status, that is, less than 20 ng/mL of 25(OH)D, was 47.3% in men and 64.5% in women.8

Vitamin D deficiency is prevalent and even more common among immigrant populations than in the general population. In a previous study, the prevalence of vitamin D deficiency was 60.0% in US immigrants from various countries.9 In an Australian study of 215 refugee children, 61% were found to have vitamin D insufficiency.10 However, owing to the heterogeneity of race, small sample size and lack of accurate health information, only a few studies have investigated the vitamin D status and associated health conditions among immigrants and refugees.

The Korean peninsula is the only divided country in the world. Since the division of Korea into south and north in 1945, differences in the socioeconomic status between


Strengths and limitations of this study

- Informative data of minority population by a researcher-driven interview and formal health examination.
- Lack of causal relationship by cross-sectional analyses.
- Single measurement of serum 25-hydroxy vitamin D level.

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the two countries have worsened. North Korea has been affected by poverty and hunger, whereas South Korea has been progressively westernised. During the past decades, the number of North Korean refugees (NKRs) has sharply increased up to approximately 24,000 by September 2012.11 Even after entering South Korea, these immigrants have been faced with many problems in stern resettlement processes and need to adjust to new cultural and socioeconomic environment12; therefore, they are still at high risk for medical, nutritional and psychological diseases.

Since 2008, we have collected demographic and medical information of NKRs living in South Korea. First, we investigated the prevalence and determinants of vitamin D status in this population. Second, although the association between vitamin D deficiency and metabolic health consequences has been widely investigated in the general population, this has rarely been done in immigrant or minority groups. Therefore, we also evaluated whether vitamin D deficiency is associated with obesity and metabolic syndrome in this group.

METHODS
Participants
This study used the data from the NORNS (North Korea refugee health in South Korea) study, which aimed to assess the health and nutritional status of 30–81-year-old NKRs living in South Korea. From October 2008, 647 NKRs voluntarily participated in the first wave survey. They participated in a structured interview, physical examination and blood sampling at the first visit to the Korea University Anam hospital located in Seoul. Since 2012, a second follow-up survey (second wave) has been conducted among NKRs who participated in the first wave survey. The second wave survey aimed to chase the changes of health and nutritional condition after adaptation to the South Korean society of NKRs.

The serum 25(OH)D level was measured in 386 participants from the first cohort. The detailed protocol and methods of the NORNS study have been reported previously.13 Written informed consent was obtained from all participants, and this study was approved by the Institutional Review Board (IRB) of Korea University’s Anam Hospital under IRB process No. ED08023.

Questionnaire
Information on general demographic data including age, sex, occupation, income, marital status, residence in North and South Korea, year of emigration from North Korea, year of entry into South Korea, and the length of residence in a third nation was included in the questionnaire. Information was obtained on medical conditions including hypertension, diabetes mellitus, dyslipidaemia, cancer, infectious disease, autoimmune disease, pulmonary disease, cardiovascular disease and medications prescribed to the participants. Information on health-related lifestyle was also obtained, including smoking (never, <5 packs of cigarette, or ≥5 packs of cigarette in the lifetime), alcohol consumption (never drinkers and current drinkers) and the amount of physical activity performed recently (none, <10 h per week, ≥10 h per week). All information in the questionnaire was self-reported.

Anthropometric and biochemical measurements
Anthropometric measurements including height, body weight and waist circumference were made after an overnight fast at the first visit. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared. Data on height and body weight at the time of emigration from North Korea and entry into South Korea were self-reported. These data allowed us to calculate the body weight changes for each participant. Systolic and diastolic blood pressure was measured using an automatic blood pressure monitor (TM-2655P; Biospace, Japan).

For the measurement of the serum 25(OH)D level, blood samples were collected from each participant after overnight fasting. Blood samples were centrifuged, immediately refrigerated, and transported in cold storage to the Neodine Reference Laboratories in Seoul, Korea. Serum 25(OH)D levels were measured using a gamma counter (1470 WIZARD, Perkin-Elmer, Finland). We defined vitamin D deficiency as a serum 25(OH)D level of less than 20 ng/mL, and vitamin D insufficiency as a 25(OH)D of 20–29 ng/mL.3 14

Serum total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol and liver enzyme levels were measured using an enzymatic method with a chemistry analyser (TBA 200-FR; Toshiba, Japan). The plasma glucose level was measured using the glucose oxidase method.

Metabolic syndrome was defined according to the Adult Treatment Panel III of the National Cholesterol Education Program guidelines,15 modified in accordance with the WHO’s proposed waist circumference (WC) cut-off points for Asians. Participants who met three or more of the following criteria were considered as having metabolic syndrome: WC ≥90 cm in men and ≥80 cm in women, serum triglyceride level ≥150 mg/dL, HDL-cholesterol levels <40 mg/dL in men and <50 mg/dL in women, impaired fasting glucose ≥100 mg/dL or antidiabetic treatment and blood pressure ≥130/85 mm Hg or treatment for hypertension.

Statistical analysis
Data are presented as mean±SD or absolute number/percentage. For non-normally distributed variables such as the triglyceride level, statistical analysis was performed after logarithmic transformation.

Baseline characteristics were compared between three groups after classification according to the vitamin D status (serum 25(OH)D level <10 ng/mL, 10–29 ng/mL and ≥30 ng/mL) using one-way ANOVA or χ² test. For the investigation of the relationship between the vitamin D status and its associated factors, variables were categorised
as follows: age was categorised into 10-year periods and BMI was classified as <18.5, ≥18.5 to <23, ≥23 to <25, and ≥25 kg/m². Seasons were categorised as spring (March–May), summer (June–August), fall (September–November) and winter (December–February).

We performed multivariate logistic regression analyses to investigate the association between vitamin D status and metabolic syndrome. Since the mean serum 25(OH)D level was very low and no participants had an optimal 25(OH)D level (≥30 ng/mL), the participants were divided into three groups according to the vitamin D status: <10, 10–20, and 20–30 ng/mL. In this analysis, three models were applied for each outcome: model 1 (adjusted for age, sex and season), model 2 (model 1 plus length of residence in South Korea and physical activity), and model 3 (model 2 plus BMI).

A p value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software V.18.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS
Among the 386 NKRs evaluated, 82 (21.0%) were men. The mean age of the participants was 43.7 ±10.6 years and the mean BMI was 22.7 ±2.7 kg/m². The mean serum 25(OH)D level was 17.4 ±4.5 ng/mL in men and 15.0 ±4.3 ng/mL in women. Baseline characteristics according to the vitamin D status are presented in Table 1. In general, the group with the lowest 25(OH)D level (<10 ng/mL) had lower BMI, body weight and height than the groups with higher 25(OH)D levels. Metabolic parameters including blood pressure and lipid profile were comparable between the three groups.

Prevalence of vitamin D deficiency and its associated factors
Prevalence of low vitamin D was very high in NKRs. No one had a sufficient level of serum 25(OH)D (≥30 ng/mL) among men and women. Participants with serum 25(OH)D levels of <10, 10–20, 20–30 ng/mL were 8.8%, 73.5%, and 12.3%, respectively (Table 1).

The proportion of participants with serum 25(OH)D levels of <10, 10–20, and >20 ng/mL, stratified by 10-year age groups and by sex, is described in Table 2. In men, the prevalence of vitamin D deficiency was lowest among the youngest age group (69.2% of 30–39 years) and tended to increase with age. However, in women, the prevalence of vitamin D deficiency was generally similar in all age groups.

Table 3 presents the prevalence of vitamin D deficiency according to season. As expected, this prevalence was lowest in the summer and highest in the winter for both sexes.

Association of vitamin D deficiency with metabolic syndrome and its components
Table 4 shows the relationship between BMI and serum 25(OH)D levels. Compared with the normal BMI group (18.5 to 23.0 kg/m²), underweight participants with BMI below 18.5 kg/m² had a significantly lower vitamin D level after adjusting for age, sex and season (p=0.036). However, the overweight (23.0 to 25.0 kg/m² of BMI) and obese (≥25.0 kg/m² of BMI) groups had similar serum 25(OH)D levels to the normal BMI group.

The association between vitamin D status and metabolic syndrome and its components was assessed using multivariate logistic regression analyses (Table 5). Compared with the group with the highest 25(OH)D level (20–30 ng/mL), the group with the lowest 25(OH)D level (<10 ng/mL) was associated more with metabolic syndrome after adjusting for potential confounders including age, sex, season, length of residence in South Korea and amount of physical activity (model 2). Even after additionally adjusting for BMI (model 3), the group with the lowest vitamin D level had a significantly higher OR for metabolic syndrome (OR, 6.37, 95% CI 1.34 to 30.33).

When the same analyses were applied to each metabolic syndrome component, the lowest 25(OH)D group was also associated with a significantly higher OR for high triglyceride (OR, 6.71, 95% CI 1.75 to 25.68), and low HDL (OR, 5.98, 95% CI 1.54 to 23.19) in model 3. However, high blood pressure and waist circumference were not significantly associated with the extremely low vitamin D status. For participants with a serum 25(OH)D level between 10 and 20 ng/mL, the OR for hyperglycaemia (or diabetes mellitus) was significantly increased.

DISCUSSION
This study clearly showed that a substantial number of NKRs in South Korea had vitamin D deficiency; the mean serum 25(OH)D level was 15.5 ng/mL. Moreover, the prevalence of low vitamin D was 87%, and no participants had an adequate vitamin D level among NKRs in this study. This high prevalence exceeds that of the general population, including South Koreans, and is comparable to that of older people who are assisted in nursing homes. In a previous study comprising the general population in South Korea, the prevalence of vitamin D deficiency; the mean serum 25(OH)D level was 17.4 ng/mL. Furthermore, North Korean workers generally wear long-sleeved shirts and broad-brimmed hats during work-hours except in summer, which limits vitamin D3 synthesis. However, their mean age of 43.7 years, lean body weight and predominantly physical labour activities do not fully explain the extremely low serum 25(OH)D levels.
The difficult circumstances that NKRs had to face should be considered when considering them in the context of vitamin D deficiency. They had an extremely low economic status while living in North Korea. Most of them experienced severe famine between 1994 and 1998. In addition, the failure of the healthcare system...
can aggravate the poor nutritional status. Therefore, we speculate that the low vitamin D status among NKRs is mainly due to the poor nutritional and medical status, particularly during their youth.

Old age, winter season, residence in urban areas, and obesity are well-known risk factors for vitamin D deficiency. In our study, these traditional risk factors did not affect vitamin D status except season and being female. In particular, obese participants (BMI of 25 kg/m² or greater) had higher mean 25(OH)D levels than normal BMI participants. In contrast, underweight participants (BMI less than 18.5 kg/m²) had a significantly lower level of 25(OH)D. Previous studies suggest that obesity causes vitamin D deficiency via vitamin sequestration into excess adipose tissue, and population-based studies corroborate the negative association between BMI and 25(OH)D levels. The negative association was also observed in school-age children. However, a few studies involving a specific ethnic group showed that BMI did not affect the vitamin D status. In the present study, we hypothesise that BMI values reflect the nutritional status rather than the obesity status among NKRs. To clarify this hypothesis, we tested the effect of other obesity measures, including waist circumference and percent body fat; however, these measures had no significant association with 25(OH)D levels. In contrast, height, which partially reflects the nutritional status in adolescence, was significantly correlated with 25(OH)D levels in a regression analysis ($\beta$ coefficient, 0.162, p=0.001, data not presented in the context).

Furthermore, vitamin D deficiency, especially severe vitamin D deficiency (25(OH)D <10 ng/mL), was significantly associated with metabolic syndrome primarily via the increased likelihood of having high triglyceride and low HDL. A growing body of evidence suggests that vitamin D deficiency predicts the development of insulin resistance, metabolic syndrome and cardiovascular diseases. Vitamin D activity occurs through vitamin D receptors, which are abundantly expressed in various tissues, including the endothelium, vascular smooth muscle and myocardium. In addition, vitamin D deficiency and the associated secondary hyperparathyroidism also play a role in increasing the cardiovascular risk.

We observed that low BMI was associated with low 25(OH)D levels among NKRs. This result indicates that vitamin D deficiency is strongly associated with metabolic derangement beyond obesity. This result may be due to several unidentified factors, such as low muscle mass (sarcopenia) or the thrifty phenotype hypothesis, which explains the association between poor fetal and infant growth and increased risk of impaired glucose tolerance and metabolic syndrome in adult life. However, our data partially supported this hypothesis.

This study has several limitations. The first limitation is its cross-sectional design, which limited the evaluation of the causal relationship between vitamin D status and metabolic syndrome. Second, this study was based on a single measurement of the serum 25(OH)D level; therefore, other factors, such as parathyroid hormone, serum...

**Table 5** ORs for metabolic syndrome and its components according to serum 25(OH)D levels

<table>
<thead>
<tr>
<th></th>
<th>25(OH)D</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>20–30 ng/mL</td>
<td>10–20 ng/mL</td>
<td>&lt;10 ng/mL</td>
</tr>
<tr>
<td></td>
<td>(n=49)</td>
<td>(n=294)</td>
<td>(n=36)</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>Reference</td>
<td>1.72 (0.74 to 4.04)</td>
<td>2.30 (0.77 to 6.91)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>3.45 (0.97 to 12.23)</td>
<td>5.60 (1.17 to 26.88)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Reference</td>
<td>3.00 (0.85 to 10.58)</td>
<td>6.37 (1.34 to 30.33)</td>
</tr>
<tr>
<td>High BP or HTN</td>
<td>Reference</td>
<td>2.94 (1.21 to 7.19)</td>
<td>2.16 (0.67 to 6.97)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>2.40 (0.51 to 11.44)</td>
<td>3.23 (0.96 to 10.89)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Reference</td>
<td>2.94 (0.88 to 9.88)</td>
<td>2.69 (0.58 to 12.60)</td>
</tr>
<tr>
<td>High serum glucose or DM</td>
<td>Reference</td>
<td>1.52 (0.67 to 3.43)</td>
<td>0.99 (0.31 to 3.19)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>6.30 (1.63 to 24.32)</td>
<td>1.06 (0.14 to 7.77)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Reference</td>
<td>6.03 (1.57 to 23.14)</td>
<td>1.15 (0.16 to 8.37)</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>Reference</td>
<td>1.40 (0.61 to 3.17)</td>
<td>1.01 (0.33 to 3.10)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>1.79 (0.53 to 5.98)</td>
<td>0.81 (0.15 to 4.36)</td>
</tr>
<tr>
<td>High triglyceride level</td>
<td>Reference</td>
<td>1.51 (0.73 to 3.14)</td>
<td>3.65 (1.36 to 9.76)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>1.42 (0.55 to 3.68)</td>
<td>6.81 (1.78 to 26.07)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Reference</td>
<td>1.44 (0.55 to 3.72)</td>
<td>6.71 (1.75 to 25.68)</td>
</tr>
<tr>
<td>Low HDL</td>
<td>Reference</td>
<td>1.49 (0.77 to 2.89)</td>
<td>2.77 (1.09 to 7.02)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Reference</td>
<td>1.89 (0.75 to 4.74)</td>
<td>6.00 (1.55 to 23.25)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Reference</td>
<td>1.91 (0.76 to 4.80)</td>
<td>5.98 (1.54 to 23.19)</td>
</tr>
</tbody>
</table>

Model 1: Adjusted for age, sex and season.
Model 2: Adjusted for age, sex, season, smoking, length of residence in South Korea and physical activity.
Model 3: Adjusted for age, sex, season, smoking, length of residence in South Korea, physical activity and BMI.

25(OH)D, 25 hydroxy vitamin D; BP, blood pressure; DM, diabetes mellitus; HDL, high-density lipoprotein; HTN, hypertension.

Competing interests None declared.
Patient consent Obtained.
Ethics approval All participants gave written informed consent to participate. This study was approved by the Institutional Review Board (IRB) of Korea University’s Anam Hospital.
Provenance and peer review Not commissioned; externally peer reviewed.
Data sharing statement No additional data are available.

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calcium, glomerular filtration rate and vitamin D intake through diet and supplements, were not assessed.

In conclusion, vitamin D deficiency was very common among NKRs aged ≥30 years living in South Korea, with a prevalence of 87%. Despite their low BMI, the low 25(OH)D level was associated with metabolic syndrome in this population.

Further investigations are needed to compare the vitamin D status between NKRs in South Korea and matched South Koreans. In addition, the causal relationship between vitamin D deficiency and metabolic syndrome can be elucidated with a follow-up study.

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Contributors NHK participated in the design of the study and contributed to the analysis and interpretation of data. KJK and YJK analysed the data and interpretation, and wrote the first draft of the manuscripts. SGK contributed to the conception and design of the NORNS study. SHK contributed JHA and HYK contributed to the analysis and interpretation of data. HJY, JAS, NHK, KMC and SHB contributed to the interpretation of data and critical revision of the manuscript. DSC oversaw the study, provided clinical expertise and participated in revisions of the manuscript draft for intellectual content.

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Notes