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Lower Levels of Vitamin D Among Bangladeshi Immigrants with Diabetes in Greece Compared to Indigenous Greek Patients with Diabetes

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Abstract. *Aim: Vitamin D deficiency is thought to impair insulin action and glucose metabolism; however, previous studies have not examined ethnic differences. We investigated a cohort of predominantly white Greek Caucasian and Bangladeshi immigrant patients with diabetes mellitus in order assess the association between diabetes mellitus and 25-hydroxyvitamin D [25(OH)VitD]. Materials and Methods: A total of 165 patients from Bangladesh and 118 patients from Greece with diabetes were assessed for diabetes and 25(OH)VitD status. Results: The 25(OH)VitD levels of Bangladeshi patients were significantly lower compared to Greek patients (12.42±5.86 ng/ml vs. 23.06±12.36 ng/ml, $p<0.001$). Only 1.2% of Bangladeshi patients vs. 24.57% of Greek patients had sufficient levels of 25(OH)VitD (≥30 ng/ml) Conclusion: The prevalence of vitamin D deficiency is very high amongst patients with diabetes but immigrants are at greater risk. Vitamin D supplementation could be valuable in the prevention or treatment of diabetes.*

Diabetes is widely prevalent globally, and around 285 million people have diabetes and this number is expected to reach 438 million by the year 2030 (1). Vitamin D deficiency is also a globally important public health problem (2). Exposure to ultraviolet light and consumption of foods rich in fat-soluble vitamin D (*e.g.* oily sea fish, meat, and eggs) are the main sources of vitamin D and its levels can be measured by concentration of serum 25-hydroxyvitamin D [25(OH)VitD] (3).

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Non-western immigrants are at greater risk of vitamin D deficiency compared to indigenous European populations (4-7) and this may lead to differences in health. 25(OH)VitD levels are positively associated with bone mineral density, diabetes mellitus type 2, certain cancer types, infectious diseases, auto-immune diseases and cardiovascular disease (8). 25(OH)VitD levels vary with age (9), obesity (10) and Fitzpatrick skin phototype (11).

Migrants who live in Western countries seem to have lower 25(OH)VitD levels, compared not only to their white counterparts but to their native populations in their country of origin (12). Bangladeshis have mostly type V skin (as defined on the Fitzpatrick scale) which protects against the sun but also reduces absorption of ultraviolet B sunlight that is needed to produce vitamin D by the skin. On the contrary, fair-skinned individuals synthesize more vitamin D when exposed to the same radiation regime (13). Additionally, cultural practices may discourage skin exposure, and the traditional Asian diets are not rich in vitamin D-containing foods.

Geographical location and ethnicity are related to duration of exposure to sunlight, dietary intake of vitamin D_2, skin color (determined by the amount and type of melanin), clothing, and religious practices. Moreover there is a link between serum vitamin D concentrations, glucose homeostasis, and the evolution of diabetes (14) and the relationships between vitamin D status and metabolic parameters in various ethnic groups are not well-known. The aim of this study was to measure annual variation in the vitamin D status of Bangladeshi immigrants with diabetes and to compare these with a similar cohort of Greek individuals with diabetes.

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Materials and Methods

A total of 161 randomly selected immigrants with diabetes (12 with type 1 diabetes mellitus and 149 with type 2 diabetes mellitus) from Bangladesh were compared with 118 (15 with type 1 diabetes mellitus and 103 with type 2 diabetes mellitus) randomly selected Greek Caucasian patients. Patients were recruited through community outreach and hospital-based diabetes clinics between January 2012 and December 2014 over a period of time that included all seasons. In Greece, the year can be divided into two main seasons in climatological terms: The cold and rainy period lasting from mid-October until April, and the warm dry season lasting from April to mid-October. All measurements of 25(OH)VitD were, therefore, categorized into two halves of the year: the first period from mid-October until mid-April: winter period; the and second period from mid-April until mid-October: summer period.

All patients were examined by a physician at their first visit and diabetes-related information was collected, including the type of diabetes, the length of time since diagnosis. Demographic characteristics were assessed. These included age, gender, and number of years living in Greece.

A fasting venous blood sample was collected and used to determine blood glucose, A1C and serum 25(OH)VitD. All the blood examinations were performed after informed patient consent and all the necessary documents were given to the patients in their native language.

The prevalence of vitamin deficiency (<20 ng/ml), insufficiency (20≤30 ng/ml) and sufficiency (≥30 ng/ml) was estimated, as described by the Endocrine Society Clinical Practice guidelines (15). The analytical essay for the determination of total 25(OH)VitD was obtained by Roche electrochemiluminescence binding essay (ECL) on Elecsys immunoassay analyzers, Roche Diagnostics GmbH, Mannheim, state D-68305, Germany.

Exclusion criteria were photosensitivity disorder, regular use of a sunbed or sunbathing, and a history of skin cancer and serious health problems (*e.g.* terminal illness). Patients using drugs or medication known to affect bone metabolism, those recently treated for vitamin D deficiency, or those who used vitamin D supplements were also excluded.

Data were analyzed using SPSS analytical software 22 (SPSS Inc – IBM Corporation, New York, USA). Chi-square tests (for differences of proportions) and t-tests (for differences in means) were used. Variables with *p*-values of less than 0.05 were considered significant upon analysis.

Results

A total of 76 Bangladeshi patients (65 men and 11 women) and 43 (36 men and 7 women) Greek patients were recruited over the winter period and 83 (80 men and 3 women) Bangleshi patients and 71 (61 men and 10 women) Greek patients over the summer period. Patients from Bangladesh had a mean duration of living in Greece of 10.34±6.27 years. This group was younger compared with the Greek patient group (43.96±8.1 *vs*. 48.78±9.3 years old, respectively, $p=0.778$) and had a significantly earlier age at onset of diabetes (39.3±7.3 *vs*. 41.7±10.1 years old, $p=0.021$). The reported duration of diabetes for the two groups was 4.79±4.4 years for Bangladeshis and 7.36±6.29 years for the Greek group. Patients from Bangladesh had slightly worse, but not statistical significant, glycemic control as compared with Greek patients (A1C=7.76±1.5% *vs*. 7.57±1.7%, $p=0.3$).

The 25(OH)VitD levels of Bangladeshi patients were alarmingly low compared to Greek patients (12.42±5.86 *vs*. 23.06±12.36, $p<0.001$). The same pattern also occurred regarding the seasonal periods. In Bangladeshi patients, the mean level of 25(OH)VitD in winter and summer periods was 11.28±5.53 and 13.68±6.04 ng/ml, respectively, $p=0.238$. In Greek patients the mean level of 25(OH)VitD in winter and summer periods was 21.97±13.18 and 24.19±12.32 ng/ml, respectively, $p=0.728$ (Figure 1).

The prevalence of 25(OH)VitD deficiency, insufficiency and sufficiency differ significantly in two groups of patients and in Bangladeshi patients was 90.0%, 8.6% and 1.2%, respectively, while in Greek patients, the rates were 43.2, 32.2 and 24.57%, respectively (Figure 2).

Discussion

When immigrant South Asians are compared to the host populations in Europe, Canada and the United States, they had higher prevalence of diabetes mellitus (16-18) and this is also similar for the highest levels of vitamin D deficiency and insufficiency. A striking finding of this study is that only two out of 165 patients from Bangladesh (1.2%) reached sufficiency in vitamin D status.

We found the vitamin D status of Bangladeshi immigrant patients with diabetes was poor compared to the indigenous Greek patients with diabetes. Immigrants are protected against the quantity and intensity of sunlight by their dark skin types in their homelands, but this does not happen in European countries where they migrate to. The season also affects 25(OH)VitD measurements because the intensity and the amount of sunlight varies between seasons. This is why the season period of blood sampling was mentioned.

Darker skins require more sunlight to synthesize a given amount of vitamin D (13, 19). Solar radiation stimulates the production of vitamin D in the skin from 7-dehydrocholesterol. Natural foods (*e.g.* fatty fish), fortified foods (*e.g.* margarine), and supplements are other sources of vitamin D. Immigrants from South Asia usually have darker skin than Europeans and they face a higher risk of low serum 25(OH)VitD levels (13, 20). Melanin absorbs UV radiation and protects against the sun; at the same time, melanin reduces the amount of UV radiation reaching the vitamin D precursor, 7-dehydrocholesterol, in the skin, inhibiting the first step in vitamin D synthesis.

Moreover immigrants tend to work mostly indoors and do not expose themselves to sunlight as they used to do in their

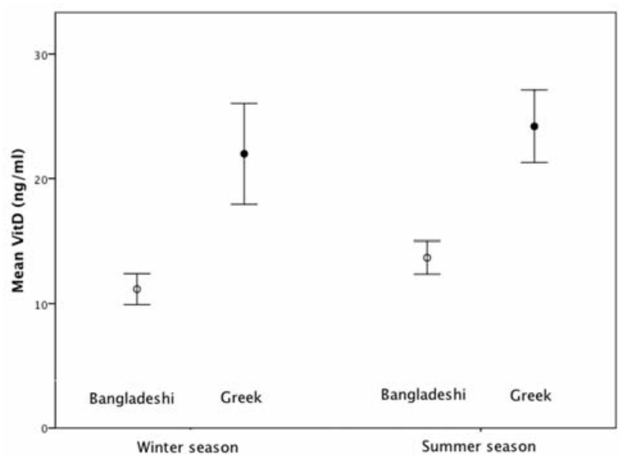

Figure 1. *Mean values of VitD levels during winter and summer period between the two groups of patients: Bangladeshi and Greek. Data are presented in error bars that represent the 95% confidence interval of a mean.*

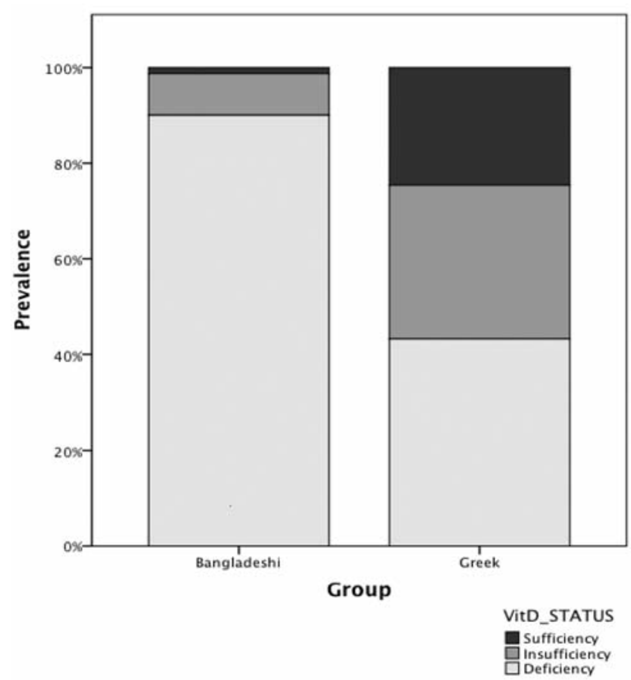

Figure 2. *Prevalence of (VitD) status among Bangladeshi and Greek patients.*

homelands. The most common occupations are shopkeepers, sellers, tailors *etc*., and more rarely do they become farmers or do other jobs that include outdoor activities. This is a main difference between rural populations with agricultural occupations and the urban population (21, 22). Poor urban housing among immigrants and large numbers of people in the household are additional factors for limited sunlight exposure. Furthermore, traditional diet patterns devoid of meat, fish and eggs, consumption of highly processed cereals, restricted access to milk and milk products, and lack of food fortification contribute to hypovitaminosis D. Likewise, Muslim women prefer to observe traditions regarding wearing of the veil, which constitutes a strong basis for no or limited sun exposure and is considered an underlying cause of higher vitamin D deficiency prevalence. In spite of the adverse health effects of vitamin D deficiency, there have been several limitations in establishing vitamin D deficiency as a public health priority compared with vitamin A, iron and iodine deficiencies in South Asian developing countries, and there is little awareness and advocacy regarding the physiological role and health consequences of vitamin D deficiency compared to other micronutrient deficiencies. Moreover, poverty and illiteracy remain two underlying determinants leading to vitamin D deficiency in many developing Asian countries.

While white-skinned Greek patients must balance the health benefits of sun protection and sun exposure, the significant minority of Bangladeshi immigrants in Greece face different issues. The risk of skin cancer is very low in South Asians (23), but their risk of low vitamin D status is higher than in Greek-born individuals.

Additionally, there is a relationship between vitamin D deficiency and development of diabetes mellitus type 2 (24-17). Vitamin D deficiency has been described in the metabolic syndrome (28). Type 1 and type 2 diabetes mellitus are considered multifactorial diseases in which both genetic predisposition and environmental factors participate in their development. Vitamin D deficiency predisposes to type 1 and type 2 diabetes development, and receptors for its activated form, 1,25-dihydroxyvitamin D_3, have been identified in β-cells and immune cells. Vitamin D deficiency has been shown to impair insulin synthesis and secretion in humans and in animal models of diabetes, suggesting its role in the development of type 2 diabetes. Furthermore, epidemiological studies suggest a link between vitamin D deficiency in early life and the later onset of type 1 diabetes (29). There is also compelling evidence that 1,25(OH)2VitD regulates β-cell function by different mechanisms, such as influencing insulin secretion by regulating intracellular levels of Ca^{2+}, increasing β-cell resistance to apoptosis, and perhaps also increasing β-cell replication. The capacity of vitamin D, more specifically 1,25(OH)2VitD, to modulate immune responses is of particular interest for both the therapy and prevention of diabetes (30). Diabetes can also reduce circulating 25(OH)VitD concentrations (31).

Because many Bangladeshi immigrants in Greece are vitamin D-deficient and at high risk of diabetes, vitamin D supplementation may contribute to preventing diabetes and insulin resistance. Recent observational data report a positive effect of vitamin D on preventing the onset of diabetes (32). Nevertheless the possible benefits of vitamin D supplementation on glycemic control are still questioned. A meta-analysis in 2012 that included longitudinal studies and randomized controlled trials reported a small enhancement in insulin resistance and fasting glucose but no positive result was seen on A1C (33). There is also a need to direct more studies to evaluating the impact of vitamin D deficiency in relation to many chronic diseases, such as diabetes, and to assessing the efficacy of supplementation and food fortification on the vitamin D status of South Asian populations.

Conclusion

This is the first study to examine the relation between 25(OH)VitD and diabetes in immigrants from Bangladesh in Greece compared to the Greek population. We found that immigrants from Bangladesh had significantly higher rates of vitamin D deficiency and insufficiency than their white counterparts.

In conclusion, the results of this study suggest that specific advice needs to be provided to people in the Bangladeshi community living in Greece. Due to lifestyle, low supplement usage, skin coloration and ambient UV at these latitudes, the general public health advice that regular short periods of sun exposure provide vitamin D sufficiency is not practical and supplements on a regular basis over the whole year could also be suggested in order to achieve sufficient levels of 25(OH)VitD.

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