The prevalence of vitamin D abnormalities in South Asians with type 2 diabetes mellitus in the UK

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Introduction

The high prevalence of both vitamin D deficiency and type 2 diabetes (T2DM) in the South Asian community in the UK is well-recognised (1–5). The additional impact of some chronic diseases on vitamin D status, such as rheumatoid arthritis, has also been described (4), although little has been published with respect to T2DM. This is surprising given the fact that vitamin D deficiency is known to be associated with beta cell dysfunction and impaired insulin secretion (6). In addition, insulin sensitivity is related to vitamin D status in healthy individuals and is independent of confounding variables including weight, central obesity and age (1). The diagnosis of hypovitaminosis D in the setting of an established chronic disease depends on both a high index of clinical suspicion in South Asian patients with musculo-skeletal symptoms and adequate biochemical investigation.

In this study, we aimed to assess and compare the prevalence of hypovitaminosis D in South Asian patients with and without T2DM and to assess the impact of vitamin D status on glycaemic control.

Patients and methods

We performed a cross-sectional study in a large tertiary referral centre in the UK. A total of 210 patients of South Asian origin were identified; 170 with and 40 without T2DM. Patients with T2DM fulfilling the entry criteria were recruited randomly from the diabetic outpatient department. The control group consisted of either healthy relatives of clinic attendees or those who were recruited from a local mosque. All study participants were more than 40 years of age, had serum creatinine < 120 µmol/l and had no evidence of hypercalcaemia (serum corrected calcium < 2.60 mmol/l). None was taking calcium or vitamin D supplements.

Serum parathyroid hormone (PTH) [normal range (NR): 10–72 ng/l], serum corrected calcium (NR: 2.05–2.60 mmol/l), phosphate (NR: 0.8–1.45...
Prevalence of hypovitaminosis D in Asian with T2DM

mmol/l), alkaline phosphatase (NR: 30–200 IU/l), urea and creatinine were all measured on the Roche modular system. HbA1c was determined using the Tosoh G7 automated glycohaemoglobin analyser (Tosoh Corporation 3-8-2, Tokyo, Japan) reporting Diabetes Control and Complications Trial (DCCT) aligned values. Serum 25-hydroxycholecalciferol D3 and D2 were measured using an isotope-dilution liquid chromatography-tandem mass spectrometry assay (7). The method was linear up to 309 nmol/l for D2 (r = 0.9977) and 314 nmol/l for D3 (r = 0.9976). Limit of quantification was 5 nmol/l for both D2 and D3 (signal-to-noise = 20). Intra-assay variation at 5 nmol/l was 25% for D2 and 21% for D3. Inter-assay variation was 10.2% and 11.0% for D2 and 4% and 11.2% for D3 at 15.6 nmol/l and 43.9 nmol/l respectively.

Vitamin D refers to 25-hydroxyvitamin D concentrations throughout this manuscript. Vitamin D deficiency was defined by serum 25-hydroxycholecalciferol values of < 12.5 nmol/l and insufficiency by values ≥ 12.5 nmol/l, but < 50 nmol/l. All patients with concentrations of < 50 nmol/l were considered to have hypovitaminosis D. Glycaemic control was taken as the average of the last three HbA1c measurements recorded in the medical records.

Statistical analysis was performed using spss 15.0 (SPSS Inc., Chicago, IL, USA). Means of continuous, normally distributed data were compared using the independent (Student’s) t-test. The Mann–Whitney test was used to compare continuous, non-normally distributed data. ANOVA and the Kruskal–Wallis test were used to compare independent, normally and non-normally distributed groups respectively. Pearson’s tests were used to correlate normally distributed continuous variables. Logistic and linear regressions were used to perform multivariate analysis and define independent predictors.

The study was approved by East Birmingham Local Research Ethics Committee and patients were consented accordingly.

Results

Demographic and biochemical data in relation to diabetes status are presented in Table 1. In our sample, 89.5% were Muslims, 6% were Sikh and 4.5% were Hindu. A majority of our sample subjects consumed meat and dairy products regularly (93%) for both. Patients with T2DM were significantly older than control subjects, but there was no significant correlation between age and log vitamin D concentrations in the diabetic cohort [correlation coefficient (CC): −0.06, p = 0.4], or the group as a whole (CC: 0.04, p = 0.6). There was no difference in the proportion of Muslims or in meat and dairy products intake between patients with and without T2DM or between men and women.

Seventy-seven per cent of patients with T2DM and 60% of control subjects respectively had their vitamin D levels measured during the spring or summer. However, the log-10 transformed vitamin D levels did not differ between subjects who had their sample in the summer or spring compared with those who had the sample in the autumn or winter (p = 0.96 and 0.24 for patients with and without T2DM respectively).

Vitamin D concentrations [median (interquartile range, IQR)] were higher in men, both in the diabetic cohort [32.8 nmol/l (21.8–43.6) vs. 23.8 nmol/l (15.2–38.9), p = 0.02] and in the group as a whole [33.2 nmol/l (21.6–47.8) vs. 22.8 nmol/l (13–39.5), p = 0.002]. The prevalence of vitamin D deficiency was higher in women (21% vs. 7%, p = 0.004) (Figure 1). This was true in both diabetic cohort (18% vs. 7%, p = 0.05) and controls (33% vs. 5%, p = 0.04).

Vitamin D concentrations in patients with T2DM compared with controls

Vitamin D concentrations were similar in patients with and without T2DM (29.6 nmol/l vs. 30.5 nmol/l respectively, p = 0.6) (Table 1). This

| Group A | Group B | p-Univariate |
|---------|---------|--------------|
| Age (years) | 63 (9) | 57 (9) | < 0.001 |
| Gender (male) | 52% | 50% | 0.862 |
| Religion (muslims) | 91% | 82% | 0.243 |
| Meat consumption | 94% | 83% | 0.336 |
| Dairy products consumption | 94% | 83% | 0.336 |
| Vitamin D deficient | 13% | 19% | 0.336 |
| Vitamin D insufficient | 70% | 51% | 0.08 |
| Vitamin D < 50 nmol/l | 83% | 70% | 0.07 |
| 25-hydroxyvitamin D (nmol/l) | 29.6 (17.4–42.2) | 30.5 (16–52) | 0.591 |

Data presented as %, mean (SD) or median (IQR) as appropriate. Vitamin D deficiency < 12.5 nmol/L. Vitamin D insufficiency 12.5<50 nmol/L. Ca, calcium; IQR, interquartile range; PTH, parathyroid hormone; SD, standard deviation; T2DM, type 2 diabetes.
remained the case even when data were analysed by the season of sampling [subjects with vs. without T2DM: 26 (17–46) vs. 44 (18–56), p = 0.22 in autumn and winter; 30 (17–41) vs. 27 (13–45), p = 0.66 in spring and summer].

There was no difference in the prevalence of vitamin D deficiency between those with and without T2DM (13% vs. 19% respectively, p = 0.34). There was, however, a trend towards more patients with vitamin D insufficiency in the diabetic cohort (70% vs. 51%, p = 0.08) and hypovitaminosis D (83% vs. 70%, p = 0.07) compared with controls. Subgroup analysis by gender showed that hypovitaminosis D was more common in men with T2DM (82.5% vs. 57.9%, p = 0.02), but not in women (84.2% vs. 83.3%, p = 0.6).

Multivariate analysis including age, gender, presence or absence of diabetes, corrected calcium, phosphate and serum PTH levels identified age [odds ratio (OR): 0.95, 95% confidence interval (CI): 0.91–0.99, p = 0.024], diabetic status (OR: 3.18, 95% CI: 1.18–8.55, p = 0.022) and serum PTH (OR: 1.03, 95% CI: 1.01–1.05, p = 0.003) as independent predictors of hypovitaminosis D. This was not affected by season.

Glycaemic control, vitamin D and parathyroid hormone

In patients with T2DM, there was no significant correlation between HbA1c and vitamin D concentrations (CC: 0.041, p = 0.621) or serum PTH (CC: −0.176, p = 0.324) and no difference in the mean HbA1c between patients with and without secondary hyperparathyroidism (7.53% ± 1.53, vs. 7.22% ± 1.51, p = 0.317).

There was no significant difference in mean HbA1c between patients with vitamin D deficiency, insufficiency or those who were replete (7.68% ± 1.31, 7.34% ± 1.46, 7.89% ± 1.78, p = 0.2). However, in women with vitamin D deficiency, mean HbA1c levels were higher (8.11 ± 1.11% vs. 7.33 ± 1.32%, p = 0.046) than the rest of the diabetic cohort. In men, where the prevalence of vitamin D deficiency was much lower, there was no such difference in HbA1c between vitamin D deficient and replete subjects. There was no difference in diabetes duration (9.5 vs. 9.4 years, p = 0.9) or age (64 vs. 63 years, p = 0.4) between men and women with T2DM to account for this difference.

A linear regression model, that included HbA1c as the dependant variable and age, corrected calcium, phosphate, serum PTH, season and vitamin D status as predictors, showed that vitamin D deficiency was independently related to HbA1c in women (p = 0.02), but not in men (p = 0.84).

Discussion

Our study confirms that hypovitaminosis D remains a major public health issue in the UK South Asian population in the 21st century. Eighty-one per cent of our cohort had inadequate vitamin D concentrations (< 50 nmol/l) and 14% were frankly deficient (< 12.5 nmol/l). However, whilst vitamin D concentrations were no lower in the diabetic cohort, our data did provide some evidence that the problem may be exaggerated in this group of patients as the prevalence of hypovitaminosis D was significantly higher in male patients with T2DM, and T2DM was an independent predictor of hypovitaminosis D.

There is no obvious explanation for the difference in hypovitaminosis D prevalence between men with and without T2DM other than the presence of T2DM particularly as meat and dairy products intake was similar between patients with and without T2DM. Although men with T2DM were older than controls (63 vs. 60 years), this difference was not significant and in the absence of any correlation between age and vitamin D concentrations in our cohort, does not explain the difference between the two groups.

Many studies have suggested that vitamin D deficiency may play a role in the development of chronic conditions such as hypertension, CVD, obesity tumours and type 1 diabetes (T1DM) (2,5,8–11). Vitamin D deficiency has also been associated with acute coronary events in men and increased mortality in the general population (12,13).

Hypovitaminosis D appears to increase the risk of developing T2DM (3,11). Vitamin D is more common in patients with T2DM compared with patients with T1DM independent of age or body mass index.
(14). Such a relationship between vitamin D and T2DM is predictable given that vitamin D deficiency has been associated with insulin resistance and impaired β cell function, both in subjects with and without diabetes (2,6,15–17), and the metabolic syndrome (2). Recent evidence from the Japanese population also suggests an association between 1,25-dihydroxy vitamin D deficiency and the presence of microvascular complications in T2DM (9,18). In addition, there is an inverse association between Vitamin D concentration and CVD events in patients with T2DM and renal impairment (19).

The benefits of vitamin D supplementation in patients with T2DM have been inadequately studied (20–23). The results are not consistent and some have included patients who were not vitamin D deficient (20–24). Whether there is a negative association between glycaemic control and vitamin D concentration thus remains unclear. Some studies have suggested this to be the case (18), and our data have demonstrated higher HbA1c levels in patients with vitamin D deficiency and that vitamin D deficiency was independently related to HbA1c in women, where the prevalence is increased compared with men. As vitamin D supplementation is simple and improvements in control of this order of magnitude are comparable with those delivered by some pharmacological agents (25), further well designed studies are warranted.

Despite many reports describing the high prevalence of hypovitaminosis D in Asian patients, hypovitaminosis D remains a major health problem (26–30). Undoubtedly, community-based health education, increased professional awareness and the judicious use of vitamin D supplements should be central to the prevention of this common, but treatable, condition. In addition, studies have shown (29,30), and our data confirm, that female patients are at particular risk.

A weakness of our study was the seasonal variation in sampling between diabetics and controls. However, there was no significant difference in vitamin D levels with regard to the season of sampling in our population and there was no difference in vitamin D levels between patients with and without T2DM regardless of the season. In addition, multivariate analysis confirmed diabetic status to be an independent predictor of hypovitaminosis D and that vitamin D deficiency is independently related to HbA1c despite including season and age in both analyses.

It is also true that patients with T2DM were older than controls. As vitamin D concentration decreases with age, this introduces a further potential source of bias. However, we could identify no correlation between vitamin D concentration and age in our cohort and diabetic status remained an independent predictor of hypovitaminosis D despite the inclusion of age in the multivariate model. Furthermore, there was no age difference between men with T2DM and controls and despite this, hypovitaminosis D was more common in men with T2DM.

In summary, our study shows a high prevalence of hypovitaminosis D in South Asians with T2DM, particularly in women. Abnormal vitamin D concentrations were more common in South Asians with T2DM compared with those without and diabetic control was inversely related to vitamin D status in South Asian women with T2DM. Our study has again highlighted that vitamin D deficiency/insufficiency remains a major public health issue in the UK South Asian population. Patients with T2DM may be at particular risk and the role of vitamin D replacement in improving glycaemic control in these patients deserves further study.

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