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RESEARCH ARTICLE

CORRELATION OF VITAMIN D AND SERUM CALCIUM LEVELS WITH TYPE 2 DIABETES MELLITUS IN NORTH INDIAN PUNJABI POPULATION

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ABSTRACT

Vitamin D deficiency is associated with insulin resistance and metabolic syndrome, both of which ultimately leads to Type 2 Diabetes mellitus. Thus evaluating the role of VDD in development of diabetes is burning topic for research. Present study was designed to find out whether there is a role of Vitamin D and Calcium homeostasis in individuals with T2DM of northwest Punjabi population and also evaluate correlation with Vitamin D, Calcium and phosphorus in normal healthy and individuals with diabetes mellitus. Our study showed females in this region were hypocalcemic as compared to males which may be due to dietary habits women consume less of dairy products as compared to men. T2DM patients had significantly lower S. Vit D, S. Calcium and S. Phosphorus levels as compared to controls. Thus prescribing Vit D and Calcium to the patients may be helpful in controlling glucose levels.

INTRODUCTION

Diabetes mellitus is the global burden. According to International Diabetes Federation (IDF) 6th edition across the world 382 million people are living with diabetes. India ranks number 2 with 65.1 million people living with diabetes. IDF predicts that by 2035 the prevalence of diabetes will rise to 592 million and out of which 109 million will be Indians.

Vitamin D has been gaining attention for its potential role in several non-skeletal health conditions including cancer, multiple sclerosis, cardiovascular disease, diabetes, bronchial asthma etc. Compared to healthy controls, subjects with T2DM have been observed to have significantly lower circulating 25(OH)D concentrations(Baynes *et al*, 1997; Scragg *et al*, 2004; Scragg *et al*, 1995). Vitamin D has been implicated in the development of T1DM due to its modulation of immune system (Hypponen *et al*, 2001). The mechanism by which vitamin D deficiency and T2DM are related is not well known. It directly as well as by regulating calcium homeostasis in body influences the insulin secretion and action of insulin in controlling blood sugar. Specifically, emerging evidence suggests a potential association of low vitamin D nutritional status with increased risk of T2DM, although the currently available data is inconsistent. Most cross-sectional and prospective studies have reported significant inverse associations of vitamin D with prevalent (Dalgard *et al*, 2011; Isaia *et al*, 2011; Scragg *et al*, 2004) and incident (Deleskog *et al* 2012; Gonzalez-Molero *et al*, 2012; Liu *et al*, 2010; Pittas *et al*, 2012; Pittas *et al* 2009; Pittas *et al*, 2006) T2DM, respectively. However, some studies have reported no association (Carnevl *et al*, 2012;; Grimnes *et al*, 2010; Kiriti *et al*, 2009; Robinson *et al* 2011; Snijder *et al* 2006).

Present study was designed to find out whether there is a role of Vitamin D and Calcium homeostasis in individuals with T2DM of northwest Punjabi population and also evaluate correlation with Vitamin D, Calcium and phosphorus in normal healthy and individuals with diabetes mellitus.

MATERIALS AND METHODS

The case control study was conducted in the OPD of medicine Department of Guru Nanak Hospital Amritsar. Total 150 subjects were enrolled in the study, of which 100 patients diagnosed with T2DM (ADA Diagnostic criteria) without renal complications were included in group A and 50 healthy individuals were included in group B (control group).

Subjects were excluded from the study if they had chronic liver disease or chronic kidney disease, are on therapy affecting vitamin D metabolism (like rifampicin, isoniazid, ketoconazole, phenytoin, etc.).

The subjects included in the study were assessed for fasting plasma glucose (FPG), serum calcium, serum phosphorus, serum vitamin D, 2 hour post prandial plasma glucose (PPG) and glycosylated haemoglobin (HbA_1C) levels. A comparison of Serum Vit D, Calcium and Phosphorus levels was done in patients of T2DM and normal individuals.

Statistical Analyses

All the above parameters were correlated and data collected was analysed using student's t test for calculating significance of variation among 2 groups and SPSS-16 software was used to calculate significance of data. p value <0.05 was considered significance.

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RESULTS

Patient disposition and characteristics

Out of 50 normal healthy individuals (25 were males and 25 were females) selected 7 individuals (3 males and 4 females) were between 31-40 years, 26 individuals (13 males and 13 females) were between 41-50 years, 13 individuals (7 male and 6 female) were between 51-60 years and 4 individuals (2 males and 2 females) were between 61-70 years of age. Similarly out of 100 patients with diabetes (53 males and 47 females) 13 (7 male and 6 female) were between 31-40 years, 34 (17 male and 17 female) were between 41-50 years, 30 (15 male and 15 female) were between 51-60 years and 23 (14 male and 9 female) were between 61-70 years of age. Majority of individuals both in control and patients groups were in the age range of 41-60 years.

Variation in serum calcium and phosphorous levels

Table 1 shows the comparison of S. Calcium and S. Phosphorus levels in normal healthy individuals and patients of T2DM under study.

Variation in Glucose (FPG and PPG levels)

Study reported that the range of FPG were 66-96 mg/dl with mean ± SD of 80.6 ± 7.8 mg/dl and 90-335 mg/dl with mean ± SD of 164.5 ± 54.4 mg/dl in healthy individuals and in patients with T2DM respectively. The range of PPG were 99-144 mg/dl with mean ± SD of 117.5 ±12 mg/dl and 115-376 mg/dl with mean ± SD of 207.2 ± 60.5 mg/dl in healthy individuals and patients with T2DM respectively. The difference between the HbA1c, FPG levels and PPG levels of normal individuals and patients with T2DM were statistically significant (p = 0.0001). Table 4 shows the FPG, PPPG and HbA1c levels of male diabetic patients distributed in 4 groups according to S. Vit D levels.

DISCUSSION

It was observed (Table 1) that difference between the mean values of S. Calcium in normal individuals and patients was significant (p<0.05). Thus the present study suggests that the patients with T2DM have significantly lower S. Calcium levels as compared to healthy controls as reported by several workers

Table 1 Overall variation in S. Calcium and S. Phosphorus levels in Normal Healthy and Patients of T2DM

Sr. No.	Individuals	N	S. Calcium conc. (mg/dl)			S.Phosphorus conc. (mg/dl)		
			Range	Mean ± SD	P value	Range	Mean ± SD	P value
1.	Normal healthy	50	7.9-10.4	8.8 ± 0.5	0.01	2.6-4.7	3.3 ± 0.4	0.01
2.	Diabetic	100	7.4-9.8	8.6 ± 0.4		2.3-4.7	3.4± 0.5	

It was observed that S Calcium and S Phosphorus levels were more in normal individuals as compared to diabetic individuals. p value obtained was 0.01 (p<0.05) which was statistically significant.

Table 2 shows the distribution of patients according to sex of T2DM and healthy individual under study according to S. Calcium and phosphorus levels.

As observed in table 1 difference between the mean values S. Phosphorus concentration of normal individuals and patients was significant (p<0.05) with patient group having comparatively lower levels than normal individuals. This observation can be correlated with observation of lower Vit D levels in diabetic patients.

It was found that out of 53 males 8 (15%) were hypocalcemic

Table 2 Variation of S. Calcium and S Phosphorus levels of male and female among diabetic and healthy individuals

Group	S. Calcium (mg/dl)/S.Phosphorus (mg/dl)	Diabetes Patient				Normal Healthy Individuals			
		Males	Females			Males		Female	
		Number	%age	Number	%age	Number	%age	Number	%age
1.	S Ca<8.5	8	15	27	57	0	0	11	44
	S P <2.5	1	2	2	4	0	0	0	0
2.	S Ca≥8.5	45	85	20	43	25	100	14	56
	S P ≥2.5	52	98	45	96	25	100	25	100
Total	S Ca	53	100	47	100	25	100	25	100
	S P	53	100	47	100	25	100	25	100

Variation in serum Vitamin D levels

The serum vitamin D levels were significantly (p = 0.003) low in patients with T2DM (7-52 mg/dl with mean ± SD of 21.8 ± 10.2 mg/dl) as compared to health individuals (9-65 mg/dl with mean ± SD of 27.6 ± 13 mg/dl).

Table 3 shows the distribution of diabetic patients and normal individual under study according to S.Vitamin D levels.

as well as Vit D deficient, 2 being severely and 6 moderately deficient and in case females 27 (56%) out of total 47 females were hypocalcemic along with Vit D deficiency. 2 female patients severly, 22 moderately and 1 mildly Vit D deficient. 2 out of 27 hypocalcemic female diabetic patients had normal Vit D levels. While in case of normal individuals none of the male was hypocalcemic but 11 (44%) out of 25females were hypocalcemic.

Table 3 Variation of Serum Vit D levels among Diabetic and normal individual

S. No.	Serum Vit D (ng/ml)		Diabetes Patient				Normal Healthy Individual			
			Males		Females		Males		Females	
			N	%age	N	%age	N	%age	N	%age
1.	≤30	<10 severe VDD	3	6	4	9	2	8	2	8
		11-20 moderate VDD	23	43	25	53	3	12	13	52
		21-30 mild VDD	17	32	7	15	11	44	4	16
2.		>30	10	19	11	23	9	36	6	24
Total			53	100	47	100	25	100	25	100

1 hypocalcemic female control had severe and 10 had moderate Vit D deficiency (Table 2).

Thus it was found that more of females in this region were hypocalcemic as compared to males which may be due to dietary habits as our society is male dominant society and women consume less of dairy products as compared to men.

Table 5 shows the FPG and PPG levels of Normal Healthy male and female controls distributed in 4 groups according to S. Vit D levels.

Table 6 shows the S. Calcium and S. Phosphorus levels of male and female diabetic patients and control distributed in 4 groups according to S. Vit D levels.

While out of 53 male patients, 1 male (2%) was hypophosphatemic and out of 47 females, 2 (4%) were hypophosphatemic (Table 2). In case of controls none of the male aswell as female was hypophosphatemic.

Out 53 male patients, 43 males (81%) were Vit D deficient, 3 being severe, 23 being moderate and 17 mildly deficient, while out of 47 females, 36 (77%) were Vit D deficient, 4 being severe, 25 moderate and 7 mildly deficient (Table 3). In case normal individuals out of 25 males, 16 (64%), 2 being severe, 3 being moderate and 11 being mildly deficient and out of 25 females, 19 (76%) were Vit D deficient, 2 being severe, 13 moderate and 4 mildly deficient (Table2). This shows that majority of both patients as well as controls under study were Vit D deficient. However in cases of males, more of the male patients as compared to normal healthy males are deficient, while in case of females there is not much difference.

Thus from this study we can come to conclusion that northwest Punjabi population is Vit D deficient which may be due to decreased synthesis of Vit D due to unfavorable angle of sun rays reaching this zone for proper synthesis.

It is general belief that due to abundant sunshine VDD is uncommon in India but now it is found that it is not true because India is a vast country extending from 8.4^{o} N latitude to 37.6^{o} N latitude. According to FAO/WHO Expert Consultation, locations around the equator i.e. between 420 N to 420 S are most physiologically relevant for Vitamin D synthesis and at least 30 min skin exposure of face and arms without sunscreen is sufficient for efficient synthesis.

Skin pigmentation is another important factor determining cutaneous vitamin D synthesis, as the absorption of UVB radiation is decreased with greater melanin content. Individuals with darker skin have a higher melanin content which absorbs UV photons and hence competes with 7-dehydrocholesterol (Clemens *et al*, 1982). Avoidance of sun exposure, covering most of one's body with clothing, and sunscreen use also reduce cutaneous vitamin D synthesis (Holick *et al*, 1989; .Matsuoka *et al* 1987).

Body composition is also a significant determinant of vitamin D levels, as numerous studies have consistently shown that those with increased adiposity have lower vitamin D levels (Arunabh *et al*, 2003; Liu *et al*, 1988; Wortsman *et al*, 2000), which is thought to be due to the sequestration of vitamin D in adipose tissue, given that it is a fat-soluble vitamin (Blum *et al*, 2007; Wortsman *et al* , 2000). A recent study, suggests that volumetric dilution as a function of body weight explains low 25(OH)D levels in those with a larger body size (Blum *et al*, 2007), which is supported by data indicating that vitamin D is stored in both adipose tissue and muscle(Anderson *et al*, 2010; Mawer *et al*, 1978).

The range of S. Vit D concentration in the normal individuals under study was 9-65 ng/ml with a mean $\pm$ S.D. of 27.6 $\pm$ 13.1 while in patients group S. Vit D concentration ranged from 7-52 ng/ml with a Mean $\pm$ S.D. of 21.8$\pm$ 10.2 (Table 3). It was observed that difference between the mean values of Serum Vit D concentration of normal individuals and patients was highly significant ($p<0.05$) with patient group having significantly lower levels than normal individuals.

Thus the study suggests that patients with T2DM have significantly lower Serum levels of Vit D as compared to healthy controls as reported by several workers in the previous studies (Anderson *et al*, 2010; Husemoen *et al*, 2012; Knekt *et al* 2008; Pittas *et al*, 2010).

It was observed (table 4 &5) that difference between the mean values of plasma glucose conc. of normal individuals and patients was highly significant ($p<0.05$) with patient group having higher FPG as well as PPG levels than normal individuals. This observation was in accordance with ADA criteria of diagnosing diabetes.

It was observed that there was not any significant difference in mean values of FPG, PPG and HbA1c values of male and female patients in different groups ($p>0.05$) (Table 4&5). This may be because all patients were under treatment but might be irregular in taking their medicines. 41% patients were those having FPG > 126 mg/dl and PPG >200 mg/dl, 34% patients had FPG > 126 mg/dl and PPG < 200 mg/dl while 25% patients were controlled diabetics with FPG < 126 mg/dl and PPPG < 200 mg/dl.

It was observed that there was significant difference in mean values of S. Calcium and S. Phosphorus of male diabetic patients distributed in different groups ($p<0.05$). This showed that S. Calcium and S. Phosphorus levels were higher in male diabetic patients having higher S. Vit D levels. (Table 6)

It was observed that there was significant difference in mean values of S Calcium female diabetic patients distributed in different groups ($p<0.05$) but there was no significant difference found in mean values of S. Phosphorus levels ($p>0.05$). This showed that S. Calcium levels were higher in female diabetic patients with higher S. Vit D levels but there was not much change observed in S. Phosphorus levels.

On statistical analysis while comparing S. Calcium levels and S. Phosphorus levels in different groups, p value obtained $p<0.05$ which was highly significant statistically (Table 6). This showed that S. Calcium and S. Phosphorus levels were higher in male controls having higher S. Vit D levels. (Table 6)

S. Calcium levels were higher in all the subjects with higher Vit D levels both in patients as well as control group. This clearly shows that Vit D is must for calcium homeostasis. However S. Phosphorus levels were higher in all the male subjects with higher Vit D levels both in patients as well as control but in female subjects both in patients as well as control group there was not much difference found (Table 6)

The present study showed that T2DM patients had significantly lower S. Vit D, S. Calcium and S. Phosphorus

Table 4 Comparison of HbA1c, FPG and PPG of male and female diabetic patients distributed according to S. Vit D levels

Groups	Vit D (ng/ml)	FPG (mg/dl)								PPG (mg/dl)						HbA1c					
		n		Range		Mean ±SD		Anova		Range		Mean ±SD		Anova		Range		Mean ±SD		ANOVA	
		M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
1.(severe VDD)	5-10	3	4	117-260	98-178	200.3±74.4	142.7±33.8	p=0.35	p=0.56	180-291	156-267	227.3±57.3	192.0±50.7	p=0.42	p=0.80	7.8-9.3	6.8-8.9	8.4± 0.7	7.9± 0.8	P=0.5	P=0.9
2.(moderate VDD)	11-20	23	25	90-276	98-335	167.2±49.6	165.8±62.2			152-376	131-332	219.4±60.9	202.6±61.4			6.2-13.1	6.4-11.2	8.3± 1.6	7.9± 1.4		
3.(mild VDD)	21-30	17	7	103-276	110-286	155±49.5	190.6±70.2			133-286	115-310	197.9±52.1	224.6±78.5			6.4-10.1	6.6-10.8	7.8±1.3	8.3±1.6		
4.(Normal)	31-70	10	11	108-234	121-240	146.1±46.9	179± 50.2			142-355		151-310	213.4±62.7			6.1-10.6	6.7-9.7	7.5 ±1.5	8.0 ±1.2		

Table 5 Comparison of FPG and PPG of male and female controls distributed according to S. Vit D levels

Groups	Vit D (ng/ml)	Male							Female						
		n	FPG (mg/dl)			PPPG (mg/dl)			n	FPG (mg/dl)			PPG (mg/dl)		
			Range	Mean±SD	Anova	Range	Mean ±SD	Anova		Range	Mean ±SD	Anova	Range	Mean ±SD	Anova
1.(severe VDD)	5-10	1	94	94	P=0.5	120	120	P=0.3	3	69-90	81±10.8	P=0.86	104-123	110.3±10.9	P=0.85
2.(moderate VDD)	11-20	4	77-96	85±8.7		102-129	117.7±11.8		10	70-89	77.5± 6.1		99- 131	113.7±10.8	
3.(mild VDD)	21-30	11	68-96	81.9±9.7		110-144	127±11.8		6	66-88	79.3 ±8.8		100-133	110.5±11.9	
4.(Normal)	31-70	9	68-92	81.1±8		100-131	118±11.7		6	72-82	77.6± 4.5		101-127	115± 9.4	

Table 6 Comparison of S. Calcium and S. Phosphorus levels of male and female diabetic individuals and controls distributed according to S. Vit D levels

Groups	Vit D (ng/ml)	Diabetic													Normal healthy individual													
		Male							Female						Male							Female						
		n	S. Calcium conc.(mg/dl)			S. Phosphorus conc. (mg/dl)		n	S. Calcium conc.(mg/dl)			S. Phosphorus conc. (mg/dl)			n	S. Calcium conc.(mg/dl)			S. Phosphorus conc. (mg/dl)			n	S.Calcium conc.(mg/dl)		S. Phosphorus conc. (mg/dl)			
			Range	Mean ±SD	Anova	Range	Mean ±SD	Anova		Range	Mean ±SD	Anova	Range	Mean ±SD	Anova		Range	Mean ±SD	Anova	Range	Mean ±SD	Anova		Range	Mean ±SD	Anova	Range	Mean ±SD	Anova
1.(severe VDD)	5-10	3	7.9-8.9	8.2±0.5	P=0.001	2.4-3.1	2.6 ±0.4	P=0.008	4	7.4-9.1	8.1 ±0.7	p=0.001	2.7-3.5	3.0±0.4	p=0.1	1	8.7	8.7	p=0.007	3.5	3.5	p=0.004	3	7.9-8.6	8.3±0.4	P=0.004	3-3.3	3.2±0.1	P=0.6
2.(moderate VDD)	11-20	23	8.0-9.4	8.7±0.4		2.7-4.1	3.3±0.4		25	7.8-9.0	8.2 ±0.3		2.3- 4.1	3.4±0.5		4	8.5-8.9	8.7±0.2		2.9- 4.0	3.6±0.5		10	8.0-8.7	8.3±0.2		2.6-3.7	3.2±0.3	
3.(mild VDD)	21-30	17	8.6-9.6	8.9±0.2		2.6-4.5	3.4±0.5		7	8.1-8.9	8.6 ±0.3		2.5-3.9	3.3 ±0.5		11	8.6-9.8	9.1±0.4		2.6-3.3	2.9±0.2		6	8.2-8.9	8.7±0.3		2.9-3.7	3.4±0.4	
4.(Normal)	31-70	10	8.5-9.8	9.1 ±0.3		2.7-4.7	3.7 ±0.6		11	8.2-9.0	8.7 ±0.3		2.7-4.7	3.7±0.6		9	9.0-10.4	9.6±0.5		2.9-3.9	3.4±0.4		6	8.5-8.9	8.7±0.2		2.7-4.7	3.5±0.8	

levels as compared to controls. It was observed that although 81% male and 77% female patients were having less than normal S. Vit D levels but only 15% males and 57% females were hypocalcemic. Similarly 64% male controls and 76% female controls were having less than normal S. Vit D levels but none of the male and 44% female controls were hypocalcemic. Thus it suggests that Vit D plays a role in calcium homeostasis in the body by increasing calcium absorption from gut, decreasing renal excretion and by bone resorption. Thus S. Calcium levels are maintained even in Vit D deficient controls as well as diabetic patients.

CONCLUSION

Result of our study suggests that Vit D and calcium may be playing role in development of diabetes .Vit D and Calcium is needed for release of insulin form the β cells of islet of Langerhans of pancreas and also for proper action of insulin is mediated if S. vit D levels are optimal. S. Calcium level is maintained by S. Vit D levels. Thus prescribing Vit D and Calcium to the patients may be helpful in controlling plasma glucose levels and also the role of exposure to sunlight for proper cutaneous synthesis of Vit D in the body should be advocated.

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Reference

Anderson JL, May HT, Horne BD, *et al*. 2010.Intermountain Heart Collaborative (IHC) Study Group. Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general healthcare population. Am J Cardiol. 106:963–8.

Arunabh S, Pollack S, Yeh J, Aloia JF.2003. Body fat content and 25-hydroxyvitamin D levels in healthy women. J. Clin. Endocrinol. Metab. 88:157-61.

Baynes KCR, Boucher BJ, Feskens EJM, and Kromhout D. 1997. Vitamin D, glucose tolerance and insulinaemia in elderly men. Diabetologia.40(3):344–7.

Blum M, Dolnikowski G, Seyoum E, Harris SS, Booth SL, Peterson J, *et al*.2008. Vitamin D (3) in fat tissue. Endocrine.33(1):90-4.

Carnevale V, Inglese M, Annese MA, De Matthaeis A, Santini SA, Frusciante V, *et al*.2012. Vitamin D and parameters of calcium homeostasis in inpatients with and without type 2 diabetes mellitus. J Endocrinol Invest.

Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. Lancet. 9;1(8263):74-6.

Dalgard C, Petersen MS, Weihe P, Grandjean P. 2011. Vitamin D status in relation to glucose metabolism and type 2 diabetes in septuagenarians. Diabetes Care. 34(6):1284-8.

Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Ostenson CG. 2012. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with normal glucose tolerance. Diabetologia. 55(6):1668-78.

Drincic AT, Armas LA, Van Diest EE, Heaney RP. 2012. Volumetric Dilution, Rather Than Sequestration Best Explains the Low Vitamin D Status of Obesity. Obesity (Silver Spring). 20(7):1444-8.

Gonzalez-Molero I, Rojo-Martinez G, Morcillo S, Gutierrez-Repiso C, Rubio- Martin E, Almaraz MC, *et al*.2012. Vitamin D and incidence of diabetes: A prospective cohort study. Clin Nutr . 31(4):571-3.

Grimnes G, Emaus N, Joakimsen RM, Figenschau Y, Jenssen T, Njolstad I, *et al*. 2010. Baseline serum 25-hydroxyvitamin D concentrations in the Tromso Study 1994-95 and risk of developing type 2 diabetes mellitus during 11 years of follow-up. Diabet Med. 27(10):1107-15.

Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. Lancet. 2(8671):1104-5.

Husemoen LL, Skaaby T, Thuesen BH,Jørgensen T, Fenger RV, Linneberg A. 2012. Serum 25(OH)D and incident type 2 diabetes: a cohort study. Eur J Clin Nutr. 66:1309–14.

Hypponen E, E. Laara E, Reunanen A, Jarvelin MR.2001. Virtanen M. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. The Lancet. 358(9292):1500–3.

Isaia G, Giorgino R, Adami S. 2001. High prevalence of hypovitaminosis D in female type 2 diabetic population. Diabetes Care . 24(8):1496.

Kirii K, Mizoue T, Iso H, Takahashi Y, Kato M, Inoue M, *et al*. 2009. Calcium, vitamin D and dairy intake in relation to type 2 diabetes risk in a Japanese cohort. Diabetologia. 52(12):2542-50.

Knekt P, Laaksonen M, Mattila C, *et al*. 2008. Serum vitamin D and subsequent occurrence of type 2 diabetes. Epidemiology. 19:666–71.

Liel Y, Ulmer E, Shary J, Hollis BW, Bell NH.1988. Low circulating vitamin D in obesity. Calcif Tissue Int. 43(4):199-201.

Liu E, Meigs JB, Pittas AG. 2010. Economos CDydroxyvitamin D score and incident type 2 diabetes in the Framingham Offspring Study. Am J Clin Nutr. 91(6):1627-33.

Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D3 synthesis. J Clin Endocrinol Metab. 64(6):1165-8.

Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury SW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. Clin Sci. 43(3):413-31.

Milner RD, Hales CN. 1967. The role of calcium and magnesium in insulin secretion from rabbit pancreas studied in vitro. Diabetologia. 3:47–9.

Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, *et al*. 2006. Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes Care. 29(3):650-6.

Pittas AG, Nelson J, Mitri J, Hillmann W, Garganta C, Nathan DM, *et al*. 2012. Plasma 25-Hydroxyvitamin D and Progression to Diabetes in Patients at Risk for Diabetes: An ancillary analysis in the Diabetes Prevention Program. Diabetes Care 2012 Mar;35(3):565-73.

Pittas AG, Sun Q, Manson JE, Dawson-Hughes B, Hu FB. 2010. Plasma 25-hydroxyvitamin D concentration and risk of incident type 2 diabetes in women. Diabetes Care. 33(9):2021-3.

Robinson JG, Manson JE, Larson J,Liu S, Song Y, Howard BV. 2011. Lack of Association Between (OH)D Levels and Incident Type 2 Diabetes in Older Women. Diabetes Care. 34(3):628-34.

Scragg, Holdaway I, Singh V, Metcalf P, Baker J, and Dryson E. 1995. Serum 25-hydroxyvitamin D3 levels decreased in impaired glucose tolerance and diabetes mellitus. Diabetes Research and Clinical Practice. 27(3):181-8.

Scragg, Sowers M, and Bell C. 2004. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third. National Health and Nutrition Examination Survey Diabetes Care.27(12):2813–8.

Snijder M, van Dam R, Visser M, Deeg D, Seidell J, Lips P.2006 To: Mathieu C, Gysemans C, Giulietti A, Bouillon R (2005) Vitamin D and diabetes. Diabetologia 48:1247-1257. Diabetologia. Jan;49(1):217-8.

Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. 2000. Decreased bioavailability of vitamin D in obesity. Am. J. Clin. Nutr.72:690-3.

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