How to Cite:
Gupta, D. K., Gupta, Y., Agarwal, P., & Sanwelka, M. (2022). A case control study on the association between vitamin d deficiency and diabetes mellitus type 2 at tertiary care hospital, Jaipur. *International Journal of Health Sciences*, *6*(S5), 11659–11669.
https://doi.org/10.53730/ijhs.v6nS5.12021

A case control study on the association between vitamin d deficiency and diabetes mellitus type 2 at tertiary care hospital, Jaipur

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Abstract---Introduction: Diabetes mellitus refers to a group of common metabolic disorders. Recently, emerging evidence has suggested a role for suboptimal vitamin D status in the etiology of T2DM. This study aimed to determine the association between Vitamin -D deficiency and type 2 Diabetes Mellitus in patients of tertiary care centre, Jaipur. Method and material: This was a hospital based descriptive type of observational study done in Department of Medicine, of a tertiary care hospital in Jaipur, Rajasthan. This study included 100 cases and 100 control. Result: There were 55% males and 45% female among study participants. Out of 200 participants, 160 (80%) subjects are vit D deficient in which 84 (42%) are cases and 76 (38%) are controls, means cases are more deficient for vit D in comparision to controls. Conclusion: Though vitamin D deficiency is prevalent in T2DM and non-diabetic control subjects, its relationship in glycation control or insulin resistance in T2DM subjects could not be confirmed in our study population. This is potentially an important finding for public health, demonstrating that improvement in vitamin D status is one of the factors responsible for better health of the individuals.

Keyword---Vitamin-D, Diabetes Mellitus, Blood sugar, Diet.

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1] The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010.[2] A recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was responsible for almost 4 million deaths in 2010 (6.8% of deaths were attributed to diabetes worldwide).[2] Based on current trends, the International Diabetes Federation projects that 438 million individuals will have diabetes by the year 2030.[1] In 2011, India had 62.4 million people with diabetes.[2]

A number of modifiable risk factors for T2DM have been identified, including physical activity[1-3], cigarette smoking [4], and diet[5-9]. Recently, emerging evidence has suggested a role for suboptimal vitamin D status in the etiology of T2DM[10,11]. To date, the majority of studies looking at the association of vitamin D with T2DM have been cross-sectional, with most finding a significant association of lower vitamin D with greater IR and β-cell dysfunction[12,13]; however some studies have also reported no association[14-16]. Indigenous populations globally such as Asians, Canadians, Native Americans and Indigenous Australians, are affected by a high prevalence of T2DM and vitamin D deficiency

[17,18]. In fact, the prevalence of T2DM in the Asian population has seen an increase over the past six decades, with particularly high rates among indians. Asian populations are at an exceptionally high risk of vitamin D deficiency as well[19]. Many factors affect the vitamin D status of Asians. As a result of darker skin pigmentation, Asian people experience less cutaneous vitamin D synthesis[20]. Low serum 25(OH)D levels may also be attributed to living in environment where there is less sunlight, resulting in limited ultraviolet B (UVB) exposure which is responsible for vitamin D synthesis in the skin[21]. Also, low mean serum 25(OH)D levels have been attributed to a shift from consuming “traditional” foods (foods that are hunted, fished, or gathered) to consuming “western” foods (foods that are store bought)[22]. Furthermore, as a consequence of changing life style there is less access to vitamin D fortified dairy products and consume vitamin D supplements less commonly[23].

Despite reports of low vitamin D status among worldwide, very less studies have examined the association of 25(OH)D with IR and β-cell dysfunction. However, results of these studies have been inconsistent[24,25]. This study aimed to determine the association between Vitamin -D deficiency and type 2 Diabetes Mellitus in patients of tertiary care centre, Jaipur.

Method and Material

This was a hospital based descriptive type of observational study done in Department of Medicine, of a tertiary care hospital in Jaipur, Rajasthan. This

study included 100 cases and 100 control. All cases were patients attending the medicine OPD or admitted in wards and were screened for inclusion and exclusion criteria.

Inclusion criteria:

- Age > 18 years and < 60 years.
- All subjects with type 2 diabetes mellitus, irrespective of duration of diabetes.
- Cases were defined on the basis of FASTING BLOOD SUGAR LEVELS AND HBA1C level as per American diabetes association guidelines for diagnosis of diabetes
- Fasting blood sugar levels were >126mg/dl
- HbA1C level >6.5%
- Willing to participate in the study

Exclusion criteria:

- Age < 21 years and > 60 years.
- Diabetic patients having overt nephropathy were excluded from the study. Nephropathy was detected on Urine spot albumin examination
- Subjects who were taking vitamin D preparations or any drugs known to interfere with vitamin D metabolism.
- Any H/O taking calcium supplements
- Past or present any history of hepatic or renal disorders

After approval of ethical committee, subjects were approached by investigator itself. After explaining the nature of the study, informed consent was taken from the subjects enrolled. Enrolled subjects were interviewed by trained research assistants in accordance with a pre-tested structured questionnaire. In this a detailed history was taken and all the subjects were carefully examined. The subject's height and weight were measured using a fixed scale and a stadiometer while subjects were standing and wearing light clothing and no shoes. The increments of height and weight were 0.01 m and 0.1 kg respectively. Body mass index (BMI) was calculated as weight (kilo-grams) divided by height (meters) squared. Healthy was defined as BMI < 25 kg/m^2, but 18.5 kg/m^2 or higher. Overweight was defined as a BMI of 25 kg/m^2 or higher but less than 30 kg/m^2; Obesity was defined as a BMI of 30 kg/m^2 or more; Underweight was defined as less than 18.5 kg/m^2. [26]

Blood Pressure was measured by Mercury sphygmomanometers. Instrument – BPMR – 120 Mercurial BP Delux, Diamond. Blood pressure was considered hypertensive if ≥140/90 mmHg.[27] VITROS R Immunodiagn*ostic Pro*ducts 25-OH Vitamin D Total Reagent Pack for the quantitative measurement of total 25-OH vitamin D in human serum using the VITROS ECi/ECiQ Immunodiagnostic Systems, the VITROS 3600 Immunodiagnostic System and the VITROS 5600 Integrated system. According to WHO guidelines Vitamin d level less than 20ng/ml considered as 'deficient' and level less than 30ng/ml considered as 'insufficient'.

Statistical Analysis

Data was recorded on a pre designed performa and was entered in excel sheet to prepare master chart. Continuous variables were summarized as mean and standard deviation while categorical variables as percentages. Unpaired T test was used for continuous variables, while for categorical variable, Chi Square test was used to analyze. P value < 0.05 was taken as significant. All statistical calculation was done by using 'Medcalc 14.0.0 version' software.

Result

During defined study period, 200 participants were enrolled for the study in which 100 subjects have diabetes which were under case group and 100 subjects were non diabetic which were under control group.

Table-1
Magnitude of cases and controls in study group

AGE (Years)	CASE				CONTROL			
	MALE		FEMALE		MALE		FEMALE	
	NO	%	N0	%	NO	%	NO	%
18-30	2	1%	4	2%	10	5%	15	7.5%
31-40	15	7.5%	13	6.5%	14	7%	17	8.5%
41-50	20	10%	13	6.5%	19	9.5%	9	4.5%
51-59	21	10.5%	12	6%	9	4.5%	7	3.5%
Total	58	29%	42	21%	52	26%	48	24%

The above table shows that there were 55% males and 45% female among study participants. 55% of study participants were more than 40 years of age whereas 45% of study participants were equal to/less than 40 years of age.

Table – 2
Sex wise comparison of case and control group

Sex	Case		Control		Total	
	No	%	no	%	No	%
Male	58	29	52	26	110	55
female	42	21	48	24	90	45

chi-square = 1.973 with 1 degree of freedom; P = 0.167

Above table shows that in study group there is 55% are males, in which 29% are in case group and 26% are in control group whereas there is 45% are females,in which 21% in case group and 24% are in control group. On application of statistical test, there was no significant difference observed with sex between the two groups (P = 0.167).

Table – 3
Distribution of vitamin D level according to sex

Sex	CASE	CONTROL
Male	20.38± 4.07	23.69± 5.28
Female	17.57 ±3.46	19.46 ±3.92

Unpaired t test P; 0.549

Above table shows Mean Vit D level is more in males both in case as well as control group as compare to females but on applying unpaired t test ,it shows there is no significance statistically.

Table – 4
Distribution of vit D level according to AGE

AGE(years)	CASE	CONTROL	P VALUE
18-30	18.23± 5.96	20.52± 4.36	2.13
31-40	17.39± 4.27	21.49± 5.64	0.78
41-50	22.53± 5.04	23.83± 3.18	1.19
50-59	19.73± 3.82	21.44± 4.09	0.54

Table – 5
Magnitude of vit D level in case and control group

VitD level	case		Control		Chi square	P value
	no	%	No	%		
<10	18	9	14	7	0.427	0.512
10-20	44	22	33	16.5	2.647	0.104
20-30	22	11	29	14.5	1.395	0.257
>30	16	8	24	12	1.997	0.383
Total	100	50	100	50		

Above table shows that Vit D level <10 ng/dl found in 9 % in cases and 7 % in controls, however after applying chi square test it is not significant statically.(p > 0.05)
Above table shows that Vit D level 10-20 ng/dl found in 22 % in cases and 16.5 % in controls, however after applying chi square test it is not significant statically.(p > 0.05)
Above table shows that Vit D level 20-30 ng/dl found in 11% in cases and 14.5 % in controls, however after applying chi square test it is not significant statically.(p > 0.05)
Above table shows that Vit D level >30ng/dl found in 8% in cases and 12 % in controls, however after applying chi square test it is not significant statically.(p > 0.05)

Table 6
Magnitude of vit D deficiency in case and control group

Vit D level ng/dl	Case		Control	
	No	%	no	%
≤ 30	84	42	76	38
> 30	16	8	24	12
Total	100	50	100	50

Chisquare = 2.485 with 1 degree of freedom; p value = 0.126

Above table shows that out of 200 participants, 160 (80%) subjects are vit D deficient in which 84 (42%) are cases and 76 (38%) are controls, means cases are more deficient for vit D in comparision to controls .but on applying chi square test it is not significant statistically.($p > 0.05$)

Discussion

The increasing incidence of T2DM is taking a great toll of health resources. This has laid a number of research studies related to lifestyle, environmental and nutritional factors in an attempt to ameliorate its burden. The diverse effect of vitamin D on glucose and calcium homeostasis[28] has made it an ideal contender to know its role in glycemic control in T2DM. In the present study, we estimated vitamin D status of diabetic subjects of the SDM hospital, Jaipur(Raj). Results show highly prevalent vitamin D deficiency in this area and inverse relationship between vitamin D status (serum 25(OH)D levels) and Type 2 DM was not found. About 80% of subjects of study population were found to be having vitamin D deficiency. Some of the previous studies from India also documented highly prevalent vitamin D deficiency [2,3]. Various factors can be attributed for this poor vitamin D status among Indians such as lack of adequate sun exposure, darker skin pigmentation, obesity, and predominantly vegetarian dietary habits.

No statistically significant difference was found in the mean values of vitamin D levels among cases and controls in the present study (19.01 ± 10.27ng/mL and 22.46 ± 11.68 ng/mL respectively). Ishida et al.[29] also observed similar findings in their study and found out that 25(OH)D and 1, 25(OH)D levels were not significantly different in diabetic patients when compared with that of controls. Scragg et al.[17] also stated that no inverse association between vitamin D status and Type 2 DM in non-Hispanic blacks was present, despite their poor vitamin D status. However, in some ethnic populations (non-Hispanic whites and Mexican Americans), the inverse association was very much evident. They conclude that this could be due to altered vitamin D endocrine system and low sensitivity to vitamin D in blacks related to ethnicity. Pittas et al.[18] in a meta-analysis have also stated that the inverse association was not very consistent between serum 25(OH)D levels and prevalent Type 2 diabetes. Inverse relationship between vitamin D status and diabetes was not found in the present study. This can be attributed to ethnic variations and highly prevalent vitamin D deficiency in this area. Possibly other factors like small sample size, cross-sectional study design, dietary habits can also be attributed for this phenomenon.

Life style factors like in-door working or working in close environment with minimum sun exposure is also likely for high prevalence of vitamin D deficiency in our population. Normal office hours in India are usually from 10am to7pm while maximum sun exposure and absorption is between 11 am to 2pm with an UV index of 7-9 required for conversion of 7-dehydrocholesterol to pre vitaminD3.[30] But this seems to be unrealistic as being a tropical country summers in India are very hot, forcing most of its people to stay indoor during this time. This results in low exposure to the sunlight contributing for very low vitamin D status in our population. Study by Macdonald etal.[31] has suggested that vitamin D status might not be the only marker of ill health, but also an indicator of life style of an individual like indoor working with restrictions of sunlight exposure, low mobility ,dietary habits that might affect long-term health. Though most of the observational studies cannot demonstrate the cause and effect related to vitamin D, lower vitamin D status might be a reflection of sedentary life style and chronic non-specific illness. It can also be argued that the people with normal levels of vitamin D are in overall good health with better lifestyle and normal weight. [32]

Nonetheless, vitamin-D supplementation was not found to be effective in reducing HbA1c as stated by Melville in his news report.[19] Our finding of absence of significant association of hemoglobin glycation with vitamin D further questions its definitive role in T2DM except for poor lifestyle in our overall population. Luoetal. also showed that within T2DMsubject,regardless of a common finding of vitamin D deficiency, low vitamin D is associated neither with increased prevalence of the metabolic syndrome, nor is there any association with glycemic control.[28]

Several mechanisms like activation of vitamin D receptor and calcium homeostasis involving impaired pancreatic-β cell function and insulin resistance in T2DM have been suggested.[10] This has been confirmed by in vitro studies in animal models suggesting its role in improving insulin sensitivity and secretion [10,28,20], though the associations between 25OH Vit D, glucose homeostasis, and insulin resistance in humans seems to be inconsistent.[20] Also a number of studies have shown a consistent inverse association between vitamin D level or vitamin D intake on the incidence of T2DM[3,4],but our study could not demonstrate such relationship. Similar observation has been made in studies from New Zealand overweight adult population and British Caucasians demonstrating a weak relationship between HbA1c and vitamin D levels.[28,29] In a recent study by Davidson etal. on subjects unknown to have diabetes failed to demonstrate the effect of vitamin D supplementation to predict the development of diabetes in pre-diabetic and those with low vitamin D level compared to placebo group.[23]As with the progression in the duration ofT2DM,the β-cell reserve attenuates[24],but in our study we could not observe significant association between HbA1c and 25OH D taking into account with the duration of type2 DM.

An Australian study by Elkassaby etal.[25] recently observed a transient improvement in glycemia in T2DM with oral D3 supplementation without change in either HbA1C or beta cell function and concluded that high dose D3 has a little or no therapeutic benefit. A similar study from UAE [33] has also reported no significant change in HbA1C levels after six month of supplementation with

vitamin D3 in vitamin D-deficient obeseT2DM patients of Emirati population. A study performed on Indian subjects residing in New Zealand [34] has shown a significant correlation between insulin sensitivity and IR and decrease in FI with vitamin D supplementation while there was a significant negative correlation between HbA1C and vitamin D levels due to supplementation in South Asian subjects in UK.[35] Though, both the studies were carried out on relatively smaller populations as compared to the one under report.

Further more, in a review by Pittas etal. It was shown at least in seven trials that vitamin D supplementation has no role on glycemic measures and HOMA-IR(as an indicator of insulin resistance)in participants with normal glucose tolerance.[36] In addition, no effect of vitamin D supplementation was evident in four out of five trials (with participants from normal glucose tolerance) that reported insulin resistance as an outcome.[36] A review study by George etal.again argued against vitamin D supplementation for improving glycemic control and insulin resistance inT2DM and non-diabetic subjects.[37]

Moreover, a recent study by Al-Shoumer etal .demonstrated the prevalence of vitamin D deficiency in insulin resistant T2DM and normal subjects, where insulin resistance was not found to be influencing the status of vitamin D.[38] Further confirming this, Kampmann etal. and Witham etal. showed that improvement in vitamin D status may increase insulin secretion but did not improve insulin resistance and HbA1C in patients with T2DM.[39,40] This is in concordance with our findings that vitamin D levels did not show any significant linear association with HOMA-IR status in T2DM cases as well as control subjects .This is possibly because the inflammatory mechanisms are extremely stimulated by the diabetic milieu or the β-cell dysfunction, and insulin resistance is more severe and less reversible by extended duration of diabetes as explained by Luo etal.[28]

Conclusion

Though vitamin D deficiency is prevalent in T2DM and non-diabetic control subjects, its relationship in glycation control or insulin resistance in T2DM subjects could not be confirmed in our study population. This is potentially an important finding for public health, demonstrating that improvement in vitamin D status is not the only factor responsible for better health of the individuals but lifestyle and dietary changes seem to play a role which will improve the over all health including hemoglobin glycation and insulin resistance along with vitamin D levels. Whether vitamin D supplementation can delay the onset of diabetes remains to be recognized. Therefore, future studies to clarify the efficacy of vitamin D supplementation in preventing diabetes and pre-diabetes are warranted, especially in populations at high risk. So population-based prospective studies and larger interventional studies using sufficiently higher doses of vitamin D over a longer period and using larger sample size should be done.

Conflict of interest: None
Financial support: None

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