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Association of Vitamin D Deficiency with Diabetic Retinopathy in Young People with Type 1 Diabetes Mellitus

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Abstract

Background: Diabetic retinopathy is among the most common diabetic complications, and is one of the leading causes of blindness in the world. Recent studies have linked vitamin D to the pathogenesis of diabetes and there is growing evidence that vitamin D can interfere with the mechanisms involved in diabetes and its complications. Despite improvements in treatment, diabetic retinopathy remains a significant complication of type 1 diabetes mellitus. Identification of early treatable predictors of diabetic retinopathy such as vitamin D deficiency, may allow more aggressive management of those at high risk. **Purpose:** To assess the association of vitamin D deficiency with diabetic retinopathy in young people with type 1 diabetes mellitus. **Design:** Observational study with case control design. **Method:** 60 young people with type 1 diabetes aged between 11 to 24 years were included in this study. Among them, 30-young people have diabetic retinopathy and 30-young people do not have diabetic retinopathy. Purposive sampling technique was applied as per inclusion criteria. Statistical analysis of the results was done by using computer-based software, SPSS version 26. P value of less than 0.05 was considered as statistically significant. **Results:** Vitamin D deficiency was present in 83% of the young people with diabetic retinopathy and in 53% without diabetic retinopathy. The mean vitamin D level in young people with and without diabetic retinopathy was 17.38 ± 3.77 ng/ml and 20.15 ± 5.06 ng/ml respectively and the difference was statistically significant (p = 0.019). Vitamin D deficiency was increased with the severity of diabetic retinopathy. Univari-

ate and multivariate logistic regression showed vitamin D deficiency was independently associated with diabetic retinopathy with a crude odds ratio of 5.69 with a p value of 0.008 and adjusted odds ratio of 16.08 with a p value of 0.002 respectively. **Conclusion:** Result of the study revealed that vitamin D deficiency was strongly associated with diabetic retinopathy in young people with type 1 diabetes mellitus.

Keywords

Vitamin D Deficiency, Type 1 Diabetes Mellitus, Diabetic Retinopathy, Young People

1. Introduction

Diabetes Mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1]. It is one of the most common non-communicable diseases [2]. Type 1 diabetes mellitus (T1DM) remains the most common form of diabetes in young people in many populations [1] [3]. Approximately 96,000 children under the age of 15 years are estimated to develop T1DM annually worldwide [2]. There has been an upward trend in the number of newly diagnosed children with T1DM in Bangladesh which is supported by the increased number of documented cases each year in Changing Diabetes in Children (CDiC) program at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder (BIRDEM) [4].

Diabetic retinopathy (DR) is the most common microvascular disease seen in young people with T1DM which is often asymptomatic in early stages but may progress to severe disease [5] [6] [7] [8] [9]. The rising number of type 1 and type 2 diabetes in children has led to an increasing number of young people at risk of a visual problem [10] [11] [12]. It is thought that at 20 years after diabetes onset, nearly all patients with T1DM and more than 60% of those with type 2 diabetes mellitus (T2DM) will develop evidence of DR on examination [13].

DR is one of the microvascular complications of DM that results from damage to retinal capillaries and venules [14] [15]. The disease initially presents as a non-neovascular form, or non-proliferative diabetic retinopathy (NPDR). Increasing damage to the retinal vasculature results in leakage from the vessel and macular oedema, and subsequent vascular sclerosis results in ischemia, angiogenesis and ultimately, retinal neovascularization or proliferative diabetic retinopathy (PDR) [13].

Several risk factors are associated with DR and among them, hyperglycemia and hypertension have the strongest association [16]. Micronutrients such as vitamin C, vitamin E and magnesium have been suggested to play a role in the pathogenesis of DR [17]. Recent research works have linked vitamin D (VD) to the pathogenesis of diabetes and there is growing evidence that vitamin D can

interfere with the mechanisms involved in diabetes and its complications [18]. Vitamin D deficiency (VDD) is found to be highly prevalent worldwide [19]. VDD is highly prevalent in type 1 and type 2 diabetes [20]. Recently, a low level of vitamin D has been found to be associated with an increased risk of diabetic complications [19]. Vitamin D receptors are expressed extensively in the retina. This evidence indicated that vitamin D might play a role in the pathogenesis of DR [21].

Vitamin D has antioxidant, anti-inflammatory and anti-proliferative functions in all areas of the body including the eyes [22]. *In vitro* and *in vivo* studies suggested that low level of chronic inflammation played an important role in the development of DR, which could induce the vascular endothelial cell damage. It has been reported that vitamin D could defend against vascular endothelial cells damage by the suppressing of inflammatory factors, thus reducing vascular proliferation which is the characteristic of DR [23]. There is considerable data to suggest that vitamin D can inhibit angiogenesis either by a direct action on endothelial cells or indirect effect through angiogenic signaling or a combination of both [22]. Vitamin D is also thought to positively regulate hypertension and blood glucose control, both of which are strong risk factors for DR [24]. It has been reported that the disruption of glucose metabolism results in microvascular disease, especially in the retina. And vitamin D could stable the glucose metabolism by increasing insulin secretion and protecting β-islet cells in the pancreas from damage [23]. Identification of early treatable predictors of DR may allow more aggressive management of those patients who are at high risk [25]. This study was aimed to investigate the association between VDD and DR and whether VDD could predict the increased risk of development and severity of DR in young people with type 1 diabetes mellitus.

2. Materials and Methods

2.1. Study Design and Place

This was an observational study with case control design. The study was performed at Department of Ophthalmology, BSMMU, Shahbagh and CDiC Pediatric Diabetes Center, BIRDEM 2 Hospital, Shegunbagicha, Dhaka from March 2019 to May 2020.

2.2. Participants

After obtaining permission and ethical approval from Institutional review board (IRB) of both BSMMU and BIRDEM, a total of 60 young people with T1DM attending Department of Ophthalmology, BSMMU and CDiC Pediatric Diabetes Center, BIRDEM 2 Hospital were included in the study. Purposive sampling technique was applied.

2.3. Selection Criteria

Inclusion criteria of case:

- Age range 11 to 24 years
- Type 1 diabetic young people with diabetic retinopathy.

Inclusion criteria of control:

- Age range 11 to 24 years
- Type 1 diabetic young people without diabetic retinopathy.

Exclusion criteria of case:

- Age < 11 and >24 years old.
- Patients with any ocular diseases other than diabetic retinopathy.
- Patients taking vitamin D or multivitamin supplementation.
- Patients with any systemic diseases other than diabetes mellitus.

Exclusion criteria of control:

- Age < 11 and >24 years old.
- Patients with any ocular diseases.
- Patients taking vitamin D or multivitamin supplementation.
- Patients with any systemic diseases other than diabetes mellitus.

2.4. Data Collection and Study Procedure

The study protocol and handling of human material and data were adhered to the tenets of the Declaration of Helsinki. Young patients attending into Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Department of Paediatric Diabetes, Bangladesh Institute of Research and Rehabilitation in diabetes, Endocrine and Metabolic Disorders (BIRDEM-2), Dhaka who were diagnosed as a case of type 1 diabetes mellitus were the study population.

Determination of the type 1 diabetes was made by the local and International Society for Pediatric and Adolescent Diabetes (ISPAD) criteria according to available clinical features and history. T1DM was diagnosed upon abrupt onset of typical symptoms of diabetes with insulin required from diagnosis, and no sign of insulin resistance - acanthosis nigricans and usually non-obese [1] [26].

Purposive sampling technique was applied to collect the sample from the study population**.** During the study period about 250 patients were examined out of them those who fulfilled the inclusion criteria were selected. All patients were informed about the nature of the study and informed written consent was taken from the patients aged 18 years and above. And for patients under 18 years of age, informed written consent was taken from their parents or guardian and assent form was collected from the patients before enrollment.

Complete clinical evaluation including history, physical examination was done to exclude any systemic disease other than DM. Relevant ocular examination, visual acuity, and slit lamp examination was done to exclude any other ocular diseases other than DR in case group and any ocular diseases in control group. Both direct and indirect ophthalmoscopic examination was done to diagnose DR and exclude other ocular diseases and findings were recorded.

Diabetic retinopathy was evaluated by examining fundus with the help of both direct and indirect ophthalmoscopy and colour fundus photography of eyes fol-

lowing dilatation of the pupil. Micro aneurysm, dot and blot haemorrhage, hard exudates, venous changes, new vessels on disc or new vessels elsewhere was considered as diabetic retinopathy on the basis of NSC (National Screening Committee) classification [27].

Disease grading protocol in National Guidelines on screening for Diabetic retinopathy in England and Wales screening programs.

Level	Equivalent disease severity level	Clinical features
Retinopathy		
R0	No retinopathy	
R1	Mild and moderate non-proliferative diabetic retinopathy	Micro aneurysms; retinal haemorrhage or exudates not within the definition of maculopathy
R2	Severe non-proliferative diabetic retinopathy	Venous beading/loop/reduplication/Intra-retinal micro vascular abnormality, multiple deep, round or blot haemorrhage
R3	Proliferative diabetic retinopathy	New vessels disc or elsewhere
Maculopathy		
M0		No maculopathy
M1		Exudate within 1-disc diameter of the center of the fovea; circinate or group of exudates within the macula; retinal thickening within 1-disc diameter center of the fovea; any micro aneurysm or haemorrhage 1-disc diameter center of the fovea only if associated with a best visual acuity of 6/12 or worse.
Photocoagulation		
P0		No photocoagulation
P1		Evidence of focal or grid laser or peripheral scatter
Unclassifiable		
U		Unobtainable/ungradable

Ocular findings were cross checked by Ophthalmologist working in the Department of Paediatric Diabetes, Bangladesh Institute of Research and Rehabilitation in diabetes, Endocrine and Metabolic Disorders (BIRDEM-2) and fundus findings and grading of diabetic retinopathy according to NSC classification were cross checked by Vitreo-Retina specialist in Department of Ophthalmology, BSMMU.

After taking informed written consent investigation procedures were explained in details to the patients. With all aseptic measures blood was collected by venipuncture from the antecubital vein of the patients.

2 ml of blood was collected in blood collection tube containing potassium

ethylenediaminetetra-acetic acid (EDTA) for estimation of HbA1c level and 4 ml of blood was collected in blood collection tube containing clot activator for estimation of Serum 25-hydroxyvitamin D (25-OHD). The blood collection tube was labeled with patient's ID and sent for analysis.

HbA1c level was measured by Capillary Electrophoresis method in Minicap Flex Piercing, Sebia, France machine in Department of Paediatric Diabetes, Bangladesh Institute of Research and Rehabilitation in diabetes, Endocrine and Metabolic Disorders (BIRDEM-2).

Before estimation of Serum 25-hydroxyvitamin D (25-OHD) blood was centrifuged and serum portion was separated. Serum 25-hydroxyvitamin D (25-OHD) was measured by Chemiluminescent Micro-particle Immuno-Assay (CMIA) method in Atellica Solution, Siemens, Germany and Alinity ci, Abbott, USA machine in Department of Biochemistry, BSMMU.

Vitamin D status was classified as follows:

- Vitamin D deficiency: <20 ng/ml
- Normal vitamin D level: 20 - 50 ng/ml

Colour Fundus Photograph (CFP) was obtained by Canon CR-2 Digital Retinal Camera, Canon, USA. Fundus photographs were stored, viewed and processed using Canon Retinal Imaging Control Software (RICS).

2.5. Statistical Analysis

Statistical analysis was carried out by using the statistical package for the social sciences version 26.0 for windows (SPSS Inc, Chicago, Illinoics, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-square test, Unpaired t test, ANOVA test and Regression analysis were used to analyze the data. P value < 0.05 was considered as statistically significant.

3. Results

In this case control study 60 participants were selected purposively according to inclusion criteria. Among them 30 participants had type 1 diabetes mellitus with diabetic retinopathy who were considered as cases and included in Group I. And 30 participants had type 1 diabetes mellitus without diabetic retinopathy who were considered as controls and included in Group II. So, the two groups were as follows:

Group-I = Case (Type 1 diabetic young people with diabetic retinopathy)

Group-II = Control (Type 1 diabetic young people without diabetic retinopathy)

Between the two groups demographic characteristics of the participants, characteristics of their diabetes mellitus and their vitamin D status were compared.

The distribution of study participants by age, sex and occupation. Here mean age of the participants having diabetic retinopathy was 21.3 ± 2.49 years and participants having no diabetic retinopathy were 19.3 ± 2.71 years. The differ-

ence of mean age between the two groups was statistically significant with a p value of 0.004. The difference of distribution by sex was not statistically significant (p = 0.067) between two groups. Most of the participants in both group were students and the difference in the distribution of occupation was not statistically significant between two groups (Table 1).

The distribution of the study participants by the characteristics of their diabetes. Mean age of onset in Group-I was 11.0 ± 2.1 years and in Group-II was 12.67 ± 1.45 years. And the difference between the two groups were statistically significant (p = 0.001). Most of the participants (63%) with retinopathy in Group-I had diabetes for more than 10 years. The difference of duration of diabetes between two groups was statistically significant with a p value of 0.0001. The difference of glycaemic control between the two groups was also statistically significant (p = 0.028) (Table 2).

The distribution of the study participants by their Vitamin D status. In Group-I 83% participants had vitamin D deficiency. In Group-II 53% participants had vitamin D deficiency. The mean vitamin D level of the participants having diabetic retinopathy was 17.38 ± 3.77 ng/ml and in participants not having any diabetic retinopathy was 20.15 ± 5.06 ng/ml. The difference between mean vitamin D level between two groups was statistically significant with a p value of 0.019 (Table 3).

The mean value of vitamin D level of the participants with different NSC grading of diabetic retinopathy. All the participants having maculopathy had vitamin D deficiency. And the difference of the mean vitamin D level of the participants having

Table 1. Distribution of study population by demographic characteristics (n = 60).

	Group-I (Case) (n = 30)		Group-II (Control) (n = 30)		*P* value
	n	%	n	%	
Age (in years)					
11 - 15	1	3	4	14	
16 - 20	8	27	13	43	
21 - 24	21	70	13	43	
Mean ± SD	21.3 ± 2.49		19.3 ± 2.71		0.004
Range (min-max)	13 - 24		14 - 24		
Sex					
Male	14	47	13	43	0.067
Female	16	53	17	57	
Occupation					
Student	20	66	25	83	
Housewife	5	17	1	3	0.188
Others	5	17	4	14	

Table 2. Distribution of study population by characteristics of diabetes (n = 60).

	Group-I (Case) (n = 30)		Group-II (Control) (n = 30)		*P* value
	n	%	n	%	
Age of onset of DM (in years)					
5 - 10	12	40	1	3	
11 - 15	18	60	27	91	
16 - 20	0	0	2	6	
Mean ± SD	11.0 ± 2.1		12.67 ± 1.45		0.001
Range (min-max)	7 - 15		10 - 16		
Duration of DM (in years)					
≥10	19	63	7	23	
<10	11	37	23	77	
Mean ± SD	10.3 ± 3.14		6.87 ± 3.14		0.0001
Range (min-max)	5 - 15		1 - 12		
Glycaemic control (HbA1c in %)					
<7	1	3	4	13	
7 - 9	5	17	11	37	
>9	24	80	15	50	
Mean ± SD	11.17 ± 2.25		9.83 ± 2.36		0.028
Range (min-max)	7.6 - 14. 7		6.4 - 14		

Table 3. Distribution of study population by Vitamin D status (n = 60).

Vitamin D (ng/ml)	Group-I (Case) (n = 30)		Group-II (Control) (n = 30)		*P* value
	n	%	n	%	
Deficiency (<20 ng/ml)	25	83	16	53	
Normal (20 - 50 ng/ml)	5	17	14	47	
Mean ± SD	17.38 ± 3.77		20.15 ± 5.06		0.019
Range (min-max)	12.1 - 27		12.1 - 28.4		

different NSC grading was statistically significant (p = 0.001) (Table 4).

Univariate and multivariate logistic regression with diabetic retinopathy as the dependent variable. Crude OR shows vitamin D deficiency, poor glycaemic control (HbA1c > 9%) and duration of diabetes more than 10 years were individually strongly associated with DR. In multivariate logistic regression after taking into consideration the effect of poor glycaemic control and duration of DM the association between vitamin D deficiency and DR became stronger with an OR of 16.08 (Table 5).

Table 4. Comparison between Vitamin D status of different NSC (National Screening Committee) grading of diabetic retinopathy (n = 60).

Variable	Univariate			Multivariate		
	Crude OR	95% CI	*P* value	Adjusted OR	95% CI	*P* value
Vitamin D deficiency (<20 ng/ml)	5.69	1.59 - 20.33	0.008	16.08	2.80 - 92.32	0.002
Glycaemic control (HbA1c > 9%)	4.00	1.27 - 12.58	0.018	6.08	1.40 - 26.38	0.015
Duration of DM (>10 years)	5.68	1.84 - 17.49	0.003	8.58	1.95 - 37.71	0.004

Table 5. Univariate and multivariate logistic regression analysis with diabetic retinopathy (case and control) as the dependent variable (n = 60).

Vitamin D status	NSC grading of diabetic retinopathy								*P* value
	R0M0		R1M0		R1M1		R2M1		
	n	%	n	%	n	%	n	%	
Deficiency (<20 ng/ml)	16	53	13	76	11	100	2	100	
Normal (20 - 50 ng/ml)	14	47	4	24	0	0	0	0	
Mean ± SD	20.15 ± 5.06		19.61 ± 3.49		14.83 ± 1.11		12.45 ± 0.49		0.001
Range (min-max)	12.10 - 28.40		16.10 - 27.0		12.9 - 16.30		12.10 - 12.80		

4. Discussion

Diabetic retinopathy is among the most common diabetes complications of DM [21]. It is also a major cause of blindness around the world [28]. Poor glycaemic control and duration of DM are some of the established risk factors for DR. Still these risk factors cannot always predict or explain the development of DR, which suggest that there may be other underlying biochemical processes that may influence the already established risk factors or the pathophysiology of DR. Vitamin D deficiency is highly prevalent in the world. Some authors go to the extend to say that there is an epidemic of VDD around the world [21]. Some non-classical functions of vitamin D has recently attracted much attention in the scientific community. Functions which are linked to the processes play a key role in the pathogenesis of DR [23] [29].

DR very rarely develops before 10 years of age [30] and ISPAD guidelines suggest to start screening for DR from age 11 years [31] and also individuals aged between 10 to 24 year are defined as young people [32] are the reasons behind choosing this age range.

Several studies have investigated the association between vitamin D deficiency and diabetic retinopathy but very few have investigated this association in type 1

diabetic young people.

In this current study, majority were females in both groups (53% with DR vs 57% without DR). Though the difference between male and female in the two groups were negligible and was statistically non-significant other studies have found that females suffer more from DM and also DR [33] [34]. Al-Agha and Ahmed (2015) [33] investigated the prevalence of VDD among children with T1DM and found that 63.8% of the participants were female. Similarly, Ahmadieh *et al.* (2013) [34] mentioned 61.3% of the participants with DM were female. But this female predominance is in case of DM not DR. So, it can be deduced that gender do not play any role in the development of DR. It should be mentioned here that the majority of young people with T1DM in Bangladesh are female as found in different studies [26] [35].

In this present study, the mean duration of DM in participants with DR was 13.9 ± 9.3 years and in participants without DR was 7.2 ± 5.5 years. The difference between the mean duration of DM between the two groups was statistically significant. Similar significant difference was also observed by Lopes *et al.* (2020) [18]; Jee, Han and Kim (2014) [36]; Long, Wang and Liu (2017) [37].

In this study, after univariate and multivariate logistic regression analysis duration of DM was found to be strongly associated with DR. The unadjusted odds ratio was 5.68 and after adjusting for other confounders the association became stronger with an adjusted odds ratio of 8.58. Zabeen *et al.* (2018) [35] found strong association of longer duration of diabetes with DR in a large cohort of 1227 young patients in Bangladesh. Shimo *et al.* (2014) [28]; Lopes *et al.* (2020) [18] and Kaur *et al.* (2011) [38] who included only participants with T1DM also found strong association between duration of DM and DR after adjusting for confounders in multivariate logistic regression.

Almost all the studies that have investigated the association between VDD and DR found poor glycaemic control to be highly associated with DR. In the present study, the mean HbA1c in participants with DR was 11.17% ± 2.25% and in participants without DR was 9.83% ± 2.36% and the difference was statistically significant ($p = 0.028$). Lopez *et al.* (2020) [18] found the mean HbA1c to be 8.5% ± 1.7% in patients with DR and 8.0% ± 1.7% in patients without DR. The difference between the findings of Lopes *et al.* (2020) [18] and the current study may be due to most of the participants of the current study were younger than the participants of Lopes *et al.* (2020) [18] study and younger age is associated with poor glycaemic control [39].

Both univariate and multivariate logistic regression analysis in the current study found HbA1c to be strongly associated with DR with a crude and adjusted odds ratio of 4.00 and 6.08 respectively. After adjusting for confounders, the association became stronger. This observation is also supported by the multivariate logistic regression analysis done in Lopes *et al.* (2020) [18]; Kaur *et al.* (2011) [38] and Zabeen *et al.* (2018) [35] studies.

ISPAD guidelines suggest to maintain HbA1c below 7% as an indication of good glycaemic control [40]. This HbA1c target is intended as an aspirational

goal, as the vast majority of children, adolescents, and young adults currently are not able to meet it. In a recent data from young adults in Norway showed peak HbA1c levels of 9.3% for girls at age 17 and 9.1% at age 19 years in males [41].

In the current study, 80% of the participants with DR had a HbA1c level above 9%, which is considered as poor glycaemic control [42]. And there was strong association between poor glycaemic control and DR on multivariate logistic regression.

In this study, vitamin D deficiency was found to be strongly associated with DR. 25 participants out of the 30 that is 83% of the participants with DR had VDD whereas only 16 out of the 30 participants that is 53% of the participants without DR had VDD. Long, Wang and Liu (2017) [37] reported that 43% of the patients with mild NPDR and 49% of the patients with severe NPDR had VDD whereas those who did not have DR, only 36% of them had VDD. Al-Agha and Ahmad (2015) [33] reported that 63.8% of the type 1 diabetic children had VDD. In the current study, similar finding was observed. 41 participants out of the 60 that is 68% of the participants enrolled in the study had VDD that is a serum 25 hydroxy vitamin D level below 20 ng/ml.

Lopes *et al.* (2020) [18] reported a mean vitamin D level of 20.3 ± 10.7 ng/ml in participants with DR and 22.7 ± 11.1 ng/ml in participants without DR. The finding of the current study shows a slightly lower mean vitamin D level in case group which was 17.38 ± 3.77 ng/ml and in control group, it was 20.15 ± 5.06 ng/ml. The difference was statistically significant ($p = 0.019$). Alcubierre *et al.* (2015) [20] showed similar findings with mean vitamin D level of 19.2 ± 10.1 ng/ml in patients with DR and 20.5 ± 8.1 ng/ml in patients without DR. The difference of mean value of vitamin D in patients with or without DR did not reach a statistical significance in Jee, Han and Kim (2014) [36] study. Most of these studies did not take the effect of seasonal variation on vitamin D status into consideration, which is well established that vitamin D level remains lower in winter season than in summer. Although a recent study showed that Asian population did not show a significant seasonal vitamin D variation [43].

In the present study, the mean vitamin D level decreased with increasing severity of DR meaning increased vitamin D deficiency was associated with severity of the DR. The difference of mean vitamin D level in different NSC grading of DR was statistically significant in this study. Alcubierre *et al.* (2015) [20] also found similar observation in their study.

Logistic regression analysis in this study showed that VDD was strongly associated with DR. Univariate logistic regression showed a crude odds ratio of 5.69 with a p value of 0.008. The association became even more stronger with an adjusted odds ratio of 16.08 with a p value of 0.002 after taking into consideration of the effect of 10 years' duration of DM on DR and poor glycaemic control defined as HbA1c more than 9%.

Poon *et al.* (2013) [25] reported that VDD was associated with 2-fold increased risk of DR. Shimo *et al.* (2014) [28]; Kaur *et al.* (2011) [38] and Lopes *et al.* (2020) [18] found that this association remained strong even after multivariate regres-

sion analysis.

The mechanism of association between vitamin D deficiency and DR can be explained by the non-classical actions of vitamin D. Multiple studies have shown that vitamin D has anti-inflammatory action, anti-angiogenic action. Both inflammatory process and angiogenesis play key role in the pathogenesis of DR. Vitamin D also helps to stabilize glucose metabolism by increasing insulin secretion and increasing insulin sensitivity [23] [29] [44]. Therefore, in a vitamin D deficiency status means lack of anti-inflammatory and anti-angiogenic support from vitamin D as well as absent of support for good glycaemic control, which ultimately leads to increased blood glucose level, increased inflammation and angiogenesis leading to DR. The association is further supported by the fact that vitamin D receptors are expressed extensively in the retina [36] and studies have proved that VDR polymorphism is associated with increased risk of retinopathy in T1DM [45].

The result of this study suggests that serum vitamin D can act as a predictor for early development of DR in young type 1 diabetic people. The result also reveals that young people with T1DM having VDD has increased risk of developing DR. So, another suggestion can be made that type 1 diabetic young people with vitamin D deficiency should be screened more frequently than usual for DR.

Limitations of the study includes multiple factors that can influence the vitamin D level are geographical and seasonal variation, ethnicity latitude was not taken under consideration and participants mostly belonged to urban population.

5. Conclusions

The purpose of this study was to evaluate the association between vitamin D deficiency and diabetic retinopathy in young people with type 1 diabetes mellitus.

Recent evidence suggests that vitamin D has anti-inflammatory and anti-angiogenic function. It also helps to maintain good glycaemic control. Lack of these non-classical functions of vitamin D in a vitamin D deficiency state can lead to development, progression and increased severity of diabetic retinopathy.

This case control study included 30 young people having type 1 diabetes mellitus with diabetic retinopathy as cases and 30 young people having type 1 diabetes mellitus without diabetic retinopathy as controls. Demographic aspects of the participants, characteristics of their diabetes mellitus and their vitamin D status were compared between the two groups.

The results of this study suggest that there is strong association of vitamin D deficiency with diabetic retinopathy in young people with type 1 diabetes mellitus. The number of participant having vitamin D deficiency in case group was much higher than in control group. With increasing severity of diabetic retinopathy, the mean vitamin D level decreased. Univariate logistic regression analysis found vitamin D deficiency to be independently associated with diabetic retinopathy and the association became stronger after multivariate logistic regres-

sion analysis. Logistic regression analysis also found poor glycaemic control and longer duration of diabetes were strongly associated with diabetic retinopathy in this study.

If a causative relationship between vitamin D deficiency and diabetic retinopathy can be established by a long term prospective study, then vitamin D deficiency can be used as a predictor of early development of diabetic retinopathy and a correction of vitamin D deficiency status which can be done by simple lifestyle modification such as exposure sunlight can delay the development of diabetic retinopathy and may also slow down the progression and severity of this blinding disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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