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Original Article

Association between Vitamin D Status and Diabetic Foot in Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Vitamin D not only perform endocrine role in body but also it have strong immunomodulatory properties. Approximately 20% of diabetic people diagnosed foot infections each year. **Objective:** To find the link between vitamin D status and diabetic foot in patients suffering from type 2 diabetes mellitus. **Methods:** A cross-sectional study conducted at the Diabetic OPD medical unit II ward 6 in Jinnah Postgraduate Medical Centre, Karachi for the duration of six months from June 2021 to May 2022. 172 patients were selected for the study and groups were divided into DF and non DF. The body mass index and age in these patients was evaluated. **Results:** The average age of patients was 67 in case of DF group and 65 in case of non DF group. There were 67 non-smokers in non DF group and 30 reported about smoking as per our data. The features like TG, TC, HDL-C, LDL-C was checked and analyzed in both groups. There were 57 patients having diabetes for more than 10 years in non DF group and 20 patients had diabetes for more than 10 years in DF group. **Conclusions:** The low serum level of vitamin D was reported in diabetic foot patients. The patients who had diabetic foot had more chance to have vitamin D deficiency as compared to control group. Therefore, low level of vitamin D is linked with diabetic foot patients significantly.

INTRODUCTION

Vitamin D not only perform endocrine role in body but also it have strong Immunomodulatory properties. It also play crucial role in calcium and bone metabolism. It is a pleotropic hormone. It has been demonstrated to be either directly or indirectly linked to an increased incidence of infections. The deficiency of vitamin D is commonly observed in the general population. Vitamin D levels are linked to a different pathologies. The pathology includes, type II diabetes and metabolic diseases [1, 2]. Peripheral diabetic neuropathy is observed in more than 50% of type 2 diabetic patients. It is one of the serious diabetic complication due to change of immune function mediators the immune state of the host being altered and it is indication of diabetic foot infection. Cytokines play crucial role in host defense mechanisms. They also aid in the macrophages differentiation, healing of wound and the eradication of infection. The inflammatory responses are trigger after the release of the inflammatory cytokines. The cytokines that trigger the inflammatory responses includes interferon (IFN), IL-1, IL-6, and TNF [3-5]. For the control of infection and effective wound healing the anti-inflammatory cytokines production is being regulated by the counter-regulatory mechanisms. These includes IL-8 and IL-10 that basically functions to avert the hyper inflammatory state. Diabetes patients suffered from abnormalities in wound-healing due to a number of known physiological factors, such as decrease in production of growth factor and impaired cytokine production [6, 7]. Different pathological conditions also disrupt the normal production of cytokines. The hyperglycemia is the one of

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the most common pathological conditions that interfere with the regular production of cytokines. The critical persistent and elevated inflammatory activities are resulted from the chronic wound development. Vitamin D deficiency has strong association with the musculoskeletal diseases. Approximately 20% of diabetic people diagnosed foot infections each year. Immunological abnormalities leads to development of diabetic foot and subsequent infections. The malfunctioning of immune cells is highly reported in the Vitamin D deficiency [8, 9]. There is a dearth of literature available on the function of systemic inflammation in patients diagnosed with diabetic foot infections in relation to vitamin D deficiency, which may be the cause of delayed wound healing. The immunological dysregulation in the vitamin D deficient patients increases the risk of developing the diabetic foot infection. Different studies have evaluated the levels of IL-1, IL-6 and TNF in the blood of patients [10].

METHODS

Patients who attended the at the Diabetic OPD medical unit II ward 6 in Jinnah Postgraduate Medical Centre, Karachi for the duration of six months from June 2021 to May 2022 were selected for the study. The data were taken from 172 patients. The patients were separated into two groups based on their clinical examination. The groups were divided into DF and non DF, there were 71 individuals present in DF group and 101 were included in the non DF group. The body mass index, age and diabetes duration in these patients was evaluated. The smoking history of patients was checked. Diabetic patients with clinical evidence of foot infection were included in the case group, while diabetic patients with no indication of any systemic infection were included in the controls group. The complete clinical history was documented on the performa. Culture positive and/or leucocytosis in the context of fever were used to diagnosis infection. All participants filled the informed written consent. This study was carried out in accordance with the Helsinki Declaration criteria. The ethical and review board committee of institute approved the study. Blood samples were collected with and without anticoagulant to calculate glycosylated HbA1c and serum 25-hydroxyvitamin D (25(OH)D). RIA commercial kit Diasorin was used to calculate serum 25(OH)D. The data was stratified. Different statistical test was performed for the analysis and SPSS version 21.0 tool was used.

RESULTS

There were 71 individuals present in DF group and 101 were included in the non DF group. Table 1 shows the basic characteristics and clinical features of two groups. The body mass index, age and duration of diabetes in these patients was evaluated. The smoking history of patients was checked. The average age of patients was 67 in case of DF group and 65 in case of non DF group. There were 43 male and 28 females in DF group, while in non DF group there were 29 male and 71 female participants. Majority of the patients were included in group who had diabetes for more than 10 years. There were 67 non-smokers in non DF group and 30 reported about smoking as per our data.

Parameter	Total n=172	DF group n=71	Non-DF group n=101	p-value
Age	65	67	65	0.001
BMI	24.3	23.1	24.3	0.005
Gender				
Male	82	43	29	<0.001
Female	90	28	71	0.001
Type 2 diabetes mellitus duration				
<5 years	55	14	24	0.001
5-10 years	32	37	19	
>10 years	85	20	57	
Smoking history				
Smoking	63	30	33	0.001
Non-smoking	109	41	67	0.001

Table 1: Basic characteristics and clinical features in two groups

The features like TG, TC, HDL-C, LDL-C was checked and analyzed as showed in the table 2. Cr (µmol/L), UA (µmol/L), Ca+2 mmol/L levels were also checked and data was compared in both groups. There were 57 patients having diabetes for more than 10 years in non DF group and 20 patients had diabetes for more than 10 years in DF group.

Features	Total	DF group n=71	Non-DF group n=101	p-value
25(OH)-VD in nmol/L	42.12	35.4	43.2	<0.001
HbA1c in %	7.98	7.9	7.8	<0.001
TG mmol/L	1.36	1.3	1.38	<0.001
TC mmol/L	4.15	3.97	4.27	<0.001
HDL-C mmol/L	1.13	1.04	1.2	<0.001
LDL-C mmol/L	2.27	2.13	2.4	<0.001
ALB g/L	41.34	38.12	43.1	<0.001
Cr (µmol/L)	72	84	65	<0.001
UA(µmol/L)	332	328	332	<0.001
Ca+2 mmol/L	2.31	2.22	2.23	<0.001

Table 2: Laboratory features in two groups

The vit D sufficiency, insufficiency and deficiency was studied in two groups, there were 33% patients having vit D deficiency in DF group as shown in table 3.

Vit D level	Total	DF group	Non- DF group
Vit D sufficiency	100%	100%	100%
Vit D insufficiency	55%	76%	52%
Vit D deficiency	24%	33%	22%

Table 3: Prevalence rate of vit-D among groups

Complications that took place because of diabetes were also evaluated and are listed in table 4.

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Features	Total n=172	DF group n=71	Non-DF group n=101	p-value
DN, n	69	39	33	<0.001
DR, n	42	29	26	<0.001
DPN, n	102	53	61	<0.001
PAD, n	45	21	17	<0.001
DAN, n	83	43	38	<0.001

Table 4: Complications due to diabetes among groups

DISCUSSION

The analysis found that the 25OH-vitamin D levels were lower in DF group (35) as compared to the non DF group (43). Also the rate of vitamin D deficiency and insufficiency was higher in the DF group as compared to the non DF group. A study was conducted to find the association of vitamin D condition and diabetic factors, it showed that the vitamin D deficiency was more in case of diabetic foot patients as compared to the non-diabetic ones [11]. The infection involved in causing diabetic foot disease is also playing role in causing vitamin D deficiency. There was an increased cytokines concentration at the inflammation site and a vitamin D deficiency of <25nmol/L was found in these patients. Since then several studies have been conducted to find the cause and link between vitamin D deficiency and diabetic foot disease [12]. However, there were inconsistent findings regarding this association. Another study has demonstrated that the serum level vitamin D deficiency has no significant link with the diabetic foot disease. A similar finding was obtained after another study carried out [13, 14]. As per previous analysis, there are several pre-clinical data studies that have shown that use of vitamin D plays a key role in healing of diabetic foot inflammation. That means vitamin D is involved in wound healing as it interacts with TGF-β signaling pathway. Another study has shown that vitamin D suppresses the NF-kB mediated inflammatory gene expression that result in decreasing the severity of inflammation [15]. Vitamin D also plays an indirect role in improving the glycemic control in case of diabetic patients. In our study the patients with poor glycemic control had less 25OH vitamin D levels as compared to the control group having normal glycemic control. These results are consistent throughout the previous studies [16]. As per pathophysiological mechanism, the patients who are suffering from type 2 diabetes mellitus have more chances to suffer from foot ulcers [17]. Moreover, the deficiency of vitamin D can be considered as a causative agent in development of ulcers in diabetes patients. Also the patients who already have diabetic foot will have low levels of vitamin D in their serum. If this levels falls for a longer period of time and it is associated with other factors like lo nutritional condition, decreased physical exercise, it can lead to limb immobilization. However, the exact mechanism by which these two factors are linked to each other is still unclear but we can say that there is some link between the diabetic foot and vitamin D deficiency [18]. In a study carried out to find the link between diabetes and vitamin D concentration in the serum, the seasonal variations of vitamin D was studied. The vitamin D levels were low in winters and in spring, however, this level was higher in summer and autumn. The study also showed that the lowering of vitamin D serum level was found in DF and non DF groups in same season. Mainly vitamin D is formed under the skin after exposure of ultraviolet B radiations. A number of factors can have role in determining the concentration of vitamin D level in the serum [19]. Therefore, there is need to screen the patients for vitamin D deficiency in winters and spring. As per previous studies there were two trails carried out where the vitamin D supply was done to check the wound healing in both groups. It was found that the vitamin D levels were restored more easily in control patients as compared to the diabetic foot patients. There is need to maintain enough vitamin D in the diet for diabetic patients so that any wound if takes place can be cured easily [20, 21]. Although this link does not exactly mean that both factors are correlated but there is a great significance in treatment and management of diabetic foot with vitamin D supplements. The sample size of our study was small so there can be confusion about the exact relationship and link between the two factors still our studies coincides with the previous studies where it was found that there was vitamin D deficiency in diabetes patients.

CONCLUSIONS

Vitamin D deficiency is a prevalent condition especially among diabetic patients. The low serum level of vitamin D was reported in diabetic foot patients. The patients who had diabetic foot had more chance to have vitamin D deficiency as compared to control group. Therefore, low level of vitamin D is linked with diabetic foot patients significantly.

Conflicts of Interest

The authors declare no conflict of interest.

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