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Vitamin D Status in Children with Type 1 Diabetes, Upper Egypt

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Abstract

Background: Type 1 diabetes Mellitus is a result of the autoimmune destruction of beta cells leading to insulin deficiency. Vitamin D deficiency may have a role in the development and pathogenesis of type-1 diabetes Mellitus by modulating immune mechanisms.

Aim of Study: Our study is a cross-sectional study aimed to assess the level of 25-hydroxy vitamin D in children with type 1 diabetes Mellitus.

Patients and Methods: Eighty patients attending the endocrinology clinic in the period from November 2016 to August 2017 were included, their ages ranged from 5 years to 15 years and all patients proved as having type 1 diabetes mellitus and were on insulin therapy. All patients were subjected to full history taking, and clinical examination in addition to the assessment of vitamin D status with measuring of serum 25-hydroxyvitamin D level in a venous blood sample.

Results: The incidence of type 1 diabetes was greater in females (65%) than in males (35%). Ages between 10-15 years were more commonly affected than the younger age group (5-10) years. Higher rates were recorded in urban than rural areas. 40% of studied children with type 1 diabetes had vitamin D deficiency but 60% of them had a sufficient level of vitamin D. Vitamin D insufficiency with type 1 DM was more common in females (83.9%), in age group (10-15) years (74%), in urban population (67%) and in children with daily consumption of junk food (64.50%). Type 1 diabetic children with vitamin D insufficiency were more liable to frequent infections and hospital admission (90%).

Conclusion: Our study concludes that vitamin D deficiency was significantly detected in type 1 diabetic children. In addition, vitamin D deficiency in these patients is associated with frequent hospital admission and complications.

Key Words: *Type 1 Diabetes – Vitamin D – Children.*

Introduction

VITAMIN D is known to be a lipid-soluble prohormone. In addition to food sources such as fatty fish, eggs, fortified milk, and cod liver oil, the human body uses ultraviolet B radiation to synthesize a significant portion of vitamin D requirements **[1]**.

There are two forms of vitamin D: vitamin D2 (ergocalciferol) and D3 (cholecalciferol). The primary role of vitamin D has been considered to be the absorption of calcium from the intestine and is necessary for skeletal health **[2]**.

Vitamin D is a global regulator of gene expression and signal transduction in virtually every tissue. In epithelial cells vitamin D, by binding with the vitamin D receptor (VDR), contributes to the maintenance of the quiescent, differentiated phenotype and protects the cells against both endogenous and exogenous stresses **[3]**.

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease induced by several immune cells and cytokines that lead to the destruction of the 0 cells within the islets of the pancreas, resulting in the dysfunction of glucose homeostasis **[4]**. Specific antibodies or molecules can be detected in the T1DM as insulin autoantibodies, autoantibodies attacking the phosphatase-related IA-2 molecule, autoantibodies againstzinc transporter, and glutamate decarboxylase 2 (GAD2; also known as GAD65). The existence of antibodies can help clinicians in the diagnosis of T1DM. In addition,

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List of Abbreviations:

BMI : Body mass index.
DCs : Dendritic cells.
ELISA : Enzyme Linked Immunosorbant Assay.
GAD : Glutamate decarboxylase.
NK : Natural killer cells.
SD : Standard deviation.
SPSS : Statistical package for social science.
T1DM : Type 1 diabetes mellitus.
VDD : Vitamin D deficiency.
VDR : Vitamin D receptor.

it is well known that T1DM has a strong association with genetic susceptibility to different environmental factors [5].

Type 1 Diabetes is linked with an imbalance of pro-/anti-inflammatory cytokines. The immune system is the main source of these cytokines and other inflammatory mediators, particularly activated T and B lymphocytes, dendritic cells (DCs), natural killer (NK) cells, and macrophages [6]. The identification of VDRs on almost all cells of the immune system, especially antigen-presenting cells and activated T lymphocytes, prompted the investigation of 1, 25(OH) dihydroxy vitamin D3 as a potential immune-modulator. Immune cells, particularly, activated macrophages and dendritic cells also contain the enzyme 1 α-hydroxylase, which is included in the conversion of vitamin D2 to vitamin D3 which is the metabolically active molecule [7].

Patients and Methods

Our study is a cross-sectional study on eighty children attending the outpatient endocrinology clinic of a children's hospital, in Egypt in the period from November 2016 to August 2017. The age of the studied children ranged from 5 years to 15 years and all patients were proven as having type 1 diabetes according to WHO diabetes diagnostic criteria (world health organization 2006) by glycated hemoglobin and glucose tolerance test and treated with insulin therapy [8]. The ethical review board faculty of medicine approved the study. The patients who participated in our study were subjected to full history taking including (age, sex, residence, family history of type 1DM, history of consumption of junk foods, hospital admission, evaluate socio-economic state (according to Abdel Twab classification) [9], in addition to full clinical examination. Morning venous blood sample (2cm) was collected and centrifuged within one hour and stored at –20°C until the time of batch analysis. Serum 25-hydroxyvitamin D 25(OH) D was measured using a competitive binding protein assay (immunodiagnostic AG, Blenheim, Germany). Levels of 25(OH) vitamin D were detected using Enzyme-Linked Immunosorbent Assay (ELISA). Interpretation of vitamin D level was based on Institute of Medicine conclusions which stated that persons are at risk of vitamin D deficiency are those having serum 25(OH)D concentrations <30nmol/L (<12ng/mL) and inadequacy at levels ranging from 30-50nmol/L (12-20ng/mL). Practically all people are sufficient at levels 50nmol/L (20ng/mL). Serum concentrations >125nmol/L (>50ng/mL) are associated with potential adverse effects [10].

Results

Table (1) shows s ocio- demographic data of studied participants. T 1 DM was more common in females than in males and in the age group (10-15) years than in the age group (5-10) years with a highly statistically significant difference. Most participants in the study were from urban areas with a highly statistically significant difference. The majority of our studied cases had normal weight and stature for age (average BMI) but without any statistically significant difference between participants in socioeconomic status and family history of type 1 DM.

Table (1): Demographic data of studied participants.

	No. (n=80)	%	*p*-value
Sex:			
Male	28	35.00	<0.001**
Female	52	65.00	
Age: (years)			
5-10	29	36.25	<0.001**
>10	51	63.75	
Residence:			
Rural	21	26.25	<0.001**
Urban	59	73.75	
Anthropometry:			
A- *BMI:*			
Underweight	1	3.75	<0.001**
Healthy weight	58	72.5	
Overweight	19	23.75	
B- *Height for age:*			
Stunted	2	2.5	<0.001**
Normal stature	78	97.5	
Socio-economic state:			
Low	21	26.25	0.083
Moderate	23	28.75	
High	36	45.00	
Family history of DM (type 1):			
Yes	38	47.50	0.635
No	42	52.50	

Table (2) shows that junk food consumption was prevalent among recruited type 1 diabetic children with a highly statistically significant difference in children with a history of daily consumption of junk food.

Table (2): Consumption of junk food in the studied participants.

	No. (n=80)	%	*p*-value
Consumption of junk food:			
No	7	8.75	<0.001**
Daily	54	67.50	
Weekly	19	23.75	

Table (3) shows the assessment of 25-hydroxy vitamin D in children with type 1 diabetes by (ng/ml). 39% of participants in the study were insufficient/deficient in vitamin D mean while 61 % of participants were Sufficient.

Table (3): 25-Hydroxy Vitamin D%

	No. (n=80)	%
Sufficient	49	61.25
Insufficient/Deficient	31	38.75
Mean ± SD	24.43±7.53	
Range	10.0-46.0	

Table (4) shows a relationship between the insufficiency of 25-hydroxy vitamin D and the socio-demographic data of recruited participants. the insufficiency of vitamin D was common in females and in the age group (10-15) years with a highly statistically significant difference. Regarding residence, most participants of the insufficient group were from urban areas with a statistically significant difference.

Table (4): Relation between insufficiency of 25-Hydroxy Vitamin D% and socio-demographic data.

	25-Hydroxy Vitamin D%		*p*-value
	Insufficient/Deficient (n=31)		
	No.	%	
Sex:			
Male	5	16.1	<.001 **
Female	26	83.9	
Age: (years)			
5-10	8	25.81	<.001 **
>10	23	74.19	
Residence:			
Rural	10	32.3	0.011 *
Urban	21	67.7	
Socio-economic state:			
Low	9	29	0.597
Moderate	9	29	
High	13	41.9	

Discussion

The etiology and natural history of T1DM are still unknown, but both genetics and environmental factors contribute to the development of T1DM **[11]**. It is reported that immune factors play a decisive role in the onset of T1DM **[12]**.

Our study revealed that type 1 diabetes was more common in females than in males. In agreement with our study, a very large study performed in Romania on 1418 recently diagnosed children with type 1 diabetes their ages between (0-14) years was stated that the incidence of type 1 diabetes was greater in girls than boys **[11]**. Other studies stated that no significant difference in incidence between males and females **[12]**. Another very large study performed in Sardinia island, Italy on 1214 children with type 1 diabetes was found that the incidence of type 1 diabetes greater in boys **[13]**. Our results can be explained by the increased incidence of autoimmune diseases in females than in males. The exact reason for that is still unknown. But many theories explained that females respond to infections, trauma, and vaccinations with increased antibody production more than males.

Our study revealed that the highest agegroupaffected with type 1 diabetes among studied children was the age group between (10-15) years. This finding agreed with the study of Karvonen et al., 2000 who stated that in most populations, the incidence rates of type 1 diabetes were increasing with age and were the highest among children aged 10-14 years **[14]**. Also, Ionescu et al., 2004 stated that the incidence of type 1 diabetes was greater in the age group between (10-14) years **[15]**. The exact reason for the increasing incidence of type 1 DM in this age group is still unknown but children in this age group were more susceptible to many environmental factors that increase the incidence to type 1 DM such as viral infections.

In our study, we noticed that no linkage between diabetes and normal growth as most participants in our study were in the normal range of weight and height for age. Other studies stated that increased BMI in childhood was an important risk factor for developing type 1 diabetes later on. This study encourages the hypothesis of beta cell stress is an important predisposing factor for type 1 diabetes as regards insulin resistance and increase weight is an important stimulant of type 1 diabetes **[16]**. On other hand other studies reported that growth was compromised in uncontrolled T1DM children and patients were significantly at risk of being short and underweight **[17]**.

In our studied cases,type 1 diabetes was found to be more common among high socioeconomic children than moderate and low socioeconomic children without statistically significant differences. According to the Socioeconomic Status Scale designed by Abd-El-Tawab 2012, 45% of studied diabetic children were of a high socioeconomic state while 29% moderate, and only 26% low

socioeconomic state. Inconsistent with our results, another study in Scotland confirmed that there was no association between type 1 and socioeconomic state [18]. Prel et al., 2007 study in Germany proved that the risk for type 1 diabetes is higher for children living in socially deprived population areas due to more exposure to pollution and infections in their environment [19].

Our study also observed that there is no significant relationship between the family history of type 1 diabetes and the development of the disease. In contrast, Anette-G. Ziegler et al., 2004 study in Germany reported that the risk of childhood diabetes in affected families was high [20]. Also, a very large study performed in Menoufia governorate, Egypt on 8000 school children aged between (6-15) years has shown that type 1 DM was common in children with a family history of type 1 DM [21].

We noticed a relationship between daily consumption of junk food and developing type 1 DM. This agrees with the study conducted by Sahoo et al., 2015 who stated that high consumption of junk food has also been associated with an increased risk of the early development of diet-related non communicable diseases, including type 1DM [22]. Another study reported that the highest diabetes rates in the world were found at Egypt and teenagers drink an alarming amount of soda making it the fattest country in Africa [23].

We observed that nearly 40% of studied children with type 1 diabetes had a deficiency in vitamin D but 60% of them had a sufficient level of vitamin D. This was in agreement with another study that stated that vitamin D was deficient in type 1 Diabetic children and in need for vitamin D supplementation [24]. Another study also showed that vitamin D levels in children at the onset of T1DM compared with children with other diseases were low [25]. Bin-Abbas et al., 2011 reported that the prevalence of vitamin D deficiency in children with diabetes was relatively high and insisted on the importance of vitamin D supplements for children with low vitamin D levels [26]. On other hand, other studies stated that the level of vitamin D in serum is not associated with the development of T1D [27].

Our study observed that insufficiency of vitamin D is more common in females than males. Some studies agreed with our results while others reported that males were more prevalent to vitamin D deficiency [28,29]. We can explain our results by that females spent more time indoors and were less exposed to sunlight which is the main source of vitamin D.

Our study revealed that vitamin D insufficiency was more common among the age group (10-15) years than the age group between 5 to 10 years. In agreed with our study results, another study conducted in Iran on school-age children 9-12 years proved that deficiency of vitamin D was more common among school-age children, and they explained their results by the less sun exposure and fewer supplementations for this age group [30] while another study proved that no association between vitamin D deficiency and certain age [31].

As regards residence, we observed that vitamin D insufficiency was more common in urban than rural children. Other studies conducted in an urban setting found a very high prevalence of vitamin D deficiency and they explained their results by more consumption of junk foods that contain low amounts of vitamin D and calcium in addition to spending more time indoors and watching TV with less physical activity [32].

We also noticed that no relation between vitamin D level and normal growth as most participants with vitamin D insufficiency in our study had a normal range of weight and height for age. Other studies agree with our results and noticed no difference in vitamin D levels in normal-weight or obese subjects [33]. Despite many emerging actions of vitamin D on skeletal, immune, cancer development, and many other body functions but to the best of our knowledge there is no relation between vitamin D deficiency and rate of growth.

According to the socioeconomic status of studied children, vitamin D insufficiency was more common among high socioeconomic children but no statistically significant difference between different socioeconomic levels. In contrast to us Hassan et al., 2015 study which was performed in Ethiopia on children aged between 11-18 years, reported that students from high socio-economic status were more likely to develop vitamin D deficiency compared to those whose families were of low socio-economic status. They explained their results by less physical activity and less sun exposure [34].

We noticed daily consumption of junk food increased the incidence of vitamin D insufficiency. This is agreed with a study that was performed on healthy adolescents aged from 15 to 18 years confirmed the correlation between fast food consumption and vitamin D deficiency [35].

Our studied children with vitamin D insufficiency were more liable to frequent hospital admission. In agreement with our results, another study stated that severe vitamin D deficiency predicts all causes of mortality in children diseased with type 1 diabetes **[36]**. Stridevi et al., 2011 also reported that low vitamin D may contribute to increased inflammation in type 1 diabetes which contributes to microvascular complications **[37]**.

Conclusions:

Vitamin D deficiencyis more common among females, Urbans, and junk food-consuming type-1 diabetic children. Deficiency of vitamin D in those patients is associated with frequent hospital admission and complications.

Ethics approval and consent to participate:

The study was approved by the ethics committee of the Faculty of Medicine, Assiut University (IBR 17100043). Written informed consents were taken from parents with explanation of benefits of the study; risks expected and suggested treatment for each case.

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مستوى فيتامين د فى الأطفال المصابين بداء السكرى من النوع الأول

الخلفية : داء السكرى من النوع الأولينتج عن تدمير المناعة الذاتية لخلايا بيتا فى البنكرياس مما يؤدى إلى نقص هرمون الأنسولين المسؤول عن التحكم فى مستوى السكر بالدم وقد يكون لنقص فيتامين (د) دور فى التسبب فى تطور هذا المرض من خلال دوره الفعال فى تنظيم آلية المناعة.

هذه دراسة مقطعية تهدف إلى تقييم مستوى ٢٥–هيدروكسى فيتامين د لدى الأطفال المصابين بداء السكرى من النوع الأول. تم إدراج ثمانين مريضاً فى عيادة الغدد الصماء فى الفترة من نوفمبر ٢٠١٦ إلى أغسطس ٢٠١٧ وتراوحت أعمارهم بين ٥ سنوات و١٥ عاماً وثبت أن جميع المرضى يعانون من مرض السكرى من النوع الأول ويتلقون العلاج بالأنسولين. تم إخضاع جميع المرضى لأخذ التاريخ الكامل والفحص السريرى بالإضافة إلى تقييم حالة فيتامين (د) عن طريق قياس مستوى مصل ٢٥ هيدروكسى فيتامين د فى عينة الدم الوريدى.

النتائج : كان نقص فيتامين د فى الأطفال المصابين بداء السكرى من النوع الأول أكثر شيوعاً عند الإناث (٨٣.٩٪) وفى الفئة العمرية (١٠–١٥) سنة (٧٤٪) وفى المناطق الحضرية (٦٧٪)، وعند الأطفال الذين يزيد الاستهلاك اليومى من الوجبات السريعة (٦٤.٥٠٪). كما كان هؤلاء الأطفال أكثر عرضة للإصابة بالعدوى المتكررة ودخول المستشفى (٩٠٪).

الخلاصة : يمكن أن نستنتج من درستنا أن نقص فيتامين (د) قد تم إكتشافه بشكل كبير فى الأطفال المصابين بداء السكرى من النوع الأول، بالإضافة إلى أن نقص فيتامين (د) فى هؤلاء المرضى مرتبط بحدوث العدوى ودخول المستشفى المتكرر وحدوث المضاعفات.