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Vitamin D status and association with glycemic control in Jordanian children with type 1 diabetes mellitus

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Abstract

Insulin shortage and the death of insulin-producing B-cells in the pancreas are symptoms of type 1 diabetes mellitus, a chronic autoimmune illness. It is among the most prevalent metabolic and endocrine disorders in children. According to international research, people with type 1 diabetes are more likely to have a vitamin D shortage or insufficiency. It has been demonstrated that giving patients vitamin D improves their glycemic control. The present study examined the link between T1DM risk variables, such as age, gender, and family history, as well as the vitamin D levels and body mass index in children with type 1 diabetes mellitus and healthy controls: 75 healthy individuals and the study included 109 individuals with type 1 diabetes mellitus; the groups were comparable in terms of BMI, age, and gender. With average ages of 8.7 ± 1.5 and 8.2 ± 1.5 and BMIs of 17.1 ± 5.1 and 16.2 ± 4.2 kg/m2, the sample comprised 45% males and 55% females. HbA1c, vitamin D, blood glucose, total cholesterol, triglycerides, liver function tests, creatinine levels, albumin, and creatinine spot urine levels have all been examined. All people (n = 109) had an average HbA1c level of 9.2%, while the control groups was 5.4%. Each group's vitamin D levels were measured to check for a relationship with HbA1c levels. 54 (72%) controls and 84 (77.7%) patients with Type 1 diabetes had vitamin D deficiency (<20 ng/mL). The low glycemic control group (HbA1c>7.5%) had significantly lower vitamin D concentrations (15/18, 83.3%; p = 0.034). The uncontrolled hyperglycemia group had a higher BMI (17±2.3) than the controlled hyperglycemia and control groups (15±2.4 and 16±4.1, respectively). The study's findings demonstrated that vitamin D levels were insufficient in both the diabetic and non-diabetic groups. Specifically, the subgroup with poor glycemic control had much lower vitamin D levels than the control group. The study also found poor adherence to vitamin D delivery, highlighting the potential advantages of supplementing infants and children with vitamin D to lower their risk of type 1 diabetes and the poor glycemic control that goes along with it.

Keywords: Vit D, Vitamin D deficiency, T1DM, Glycemic control, HbA1C, BMI, Epidemiology, prevalence, Jordan

Introduction

A number of metabolic problems Diabetes mellitus (DM) is a chronic disease that can be caused by environmental or genetic factors. [1]. High blood glucose levels are a hallmark of diabetes weight loss, polyuria, polyphagia, and poor visual acuity as a result of diminished insulin effectiveness, secretion or both. [2]. Damage to the macrovascular and microvascular systems as well as major long-term consequences might arise from persistently high blood glucose levels. Such damage may affect organs and systems and may have an effect on the kidneys, eyes, heart, blood vessels, and nerves, or may lead to severe complications such as increased risk of foot ulcers, limb amputations, renal failure, loss of vision, cardiovascular diseases, and neuropathy.[3].

Diabetes has drastically increased in prevalence worldwide in recent decades, and it is now regarded one of the most common endocrine illnesses [4,22]. According to global estimates from the International Diabetes Federation (IDF), 463 million cases of Diabetes Mellitus were recorded in 2019, either undiagnosed or diagnosed. By 2030 and 2045, this amount is expected to rise to 578 and 700 million, respectively. These estimations are most likely the result of increased sedentary lifestyles and dietary changes that include increased food intake [5,6]. Between 1998 and 2017, the prevalence of diabetes mellitus rose significantly, according to research from Jordan's The National Center for Genetics, Diabetes, and Endocrinology.

Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), and Diabetes Mellitus during pregnancy are the three forms of the disease. [7]. The death of the pancreatic B-cells that make insulin results in insulin insufficiency, the characteristic of type 1 diabetes that leads to hyperglycemia.

T1DM incidence rises by about 3% each year and varies widely by location and ethnicity. T1DM is one of the most common metabolic and endocrine illnesses affecting children, particularly [8,23].

Most T1DM patients are thought to have

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pathophysiology resulting from autoimmune loss of B-cell function, which includes humoral and cellular components and ultimately leads to B-cell death and suppression of insulin secretion, however the precise cause is unknown [9]. Additionally, the pathophysiology of this organ-specific autoimmune illness has been connected to APC, which includes dendritic cells, B-lymphocytes, and autoreactive autoantibodies against glutamic acid decarboxylase (GAD) B-cells [8].In certain cases, T1DM is idiopathic, which means that no autoantibodies or immunological response are found. In this case, idiopathic T1DM has a strong genetic relationship to HLA variables [10].

Recent research has linked serum vitamin D levels to three types of diabetes mellitus: Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), and pregnancy-related diabetes mellitus [7]. Diabetes, impaired glucose tolerance, and gestational diabetes are all brought on by the death of the pancreatic B-cells that make insulin, which results in insulin insufficiency, a symptom of type 1 diabetes that results in hyperglycemia. [12]. A significant number of children with poor diabetes control had low vitamin D levels, which is clinically relevant [13]. Pancreatic B-cells include vitamin D receptors, which control their activity. [14]. According to research on animals, active vitamin D may help stop TIDM from developing. Both vitamin D deficiency insulin tolerance and islet cell vitamin D insufficiency are prevalent. It has been demonstrated that giving non-obese subjects pharmacological dosages of 1,25(OH)2 D lowers their risk of developing diabetes and insulitis [16]. Investigating the relationship between vitamin D levels in serum among kids with type 1 diabetes mellitus while also taking demographics and non-dietary factors into consideration is the aim of this study.

Materials and Methods

Study design

The current study correlated vitamin D levels in type 1 diabetes and healthy controls with body mass index (BMI) and compared the serum levels of 25-hydroxy vitamin D, or 25(OH)D, in these youngsters to those of their healthy counterparts. Additionally, to look at the connection between a number of traits, such as age, gender, and family history, and the onset of type 1 diabetes. Prospective case-control research was conducted using this experimental approach.

Following the recommended paired characteristics, the outcomes of two existing groups of children in Jordan were compared. The first group was given the same care as the second group, which was confirmed by glycated hemoglobin (HbA1c), serum glucose, and medical history, and was healthy and without type 1 diabetes which is the disease of interest.

Subjects with TIDM and healthy control subjects were recruited from the database of the Precision Medical Labs group (PMLAB) in Amman, Jordan, and were aged 16 years and under. Approval was obtained from the research department of PMLAB, and all subjects received informed consent.

Children and adolescents in the second analysis were drawn from a meta-analysis of two existing groups of Jordanian children and adolescents. The children and adolescents were recruited using the defined inclusion and exclusion criteria.

The first group was given the same care as the second group, which was confirmed by glycated hemoglobin (HbA1c), serum glucose, and medical history, and was healthy and without type 1 diabetes which is the disease of interest .

Inclusion criteria

- Jordanian patients only.
- Type 1 diabetes mellitus has been clinically diagnosed and confirmed.
- Disease diagnosis duration of more than one year.
- Age less than 16 years.
- Parental or guardian capacity and willingness to provide consent.

Exclusion criteria

- Children and adolescents with T1DM who had the disease for less than a year were not included in the study because they might go into partial remission and display a different immunologic profile from patients who had the disease for more than a year.
- History of other chronic or autoimmune diseases
- Evidence of established renal failure

- Evidence of established liver failure
- History or current diagnosis of any kind of malignancy
- Presently taking vitamin D supplements
- severe lack of vitamin D (less than 10 µg/ml)

A questionnaire created to fulfill the objectives of this study was used to gather demographic information and medical history (Appendix).

2. Samples collection and methods

A total number of 190 participants (including 81 controls and 109 patients with the disease of interest) participated in this study and selected randomly from the PMLAB patients' database. 180 patients out of 207 consented to participate in this study with a total of (87%) participation rate. Sample collection procedures were between the periods - and -

Venous blood samples were collected in one whole blood sample using an EDTA tube, serum using a plain tube, and urine samples using a sterile plain container were collected from each participant. Following the collection of whole blood samples, EDTA samples were placed in a refrigerator at -4 °C for seven days in order to assess the HPLC method (BIORAD-D10) to determine the HbA1c values, which quantify the proportion of glycated hemoglobin bound to the blood's red blood cells. Before analysis, serum samples were kept in a freezer at -80 °C after centrifugation at 5000 rpm for seven minutes Vitamin D, blood glucose, total cholesterol, triglycerides, liver function tests, and creatinine levels were measured in these serum samples. Sterile urine containers were used to collect random urine samples to evaluate creatinine and albumin levels in urine on the same day of collection.

Based on standardized interviews with certified laboratory technicians regarding their sociodemographic information, including age, gender, nationality, educational attainment, place of residence, and other facts, the questionnaire was developed to achieve the study's goals. Additionally, it evaluated traits including height, weight, family history, amount of exercise, and duration of solar exposure. Accurate weight and height measurements were used to compute the weight (KG) divided by the square of the height (m) yields the body mass index (BMI). Furthermore, data was gathered on feeding practices, vitamin D supplementation, nutritional intake, and past and present health issues. The connection between glycemic management and vitamin D levels as determined by HbA1c levels was examined. For statistical analysis, SSPS software was used.

Results

Six control participants—two men and four women—were disqualified from the final study. Three of them were disqualified because they had a history of other chronic illnesses, two were disqualified because they currently had various cancer diagnoses, and one was disqualified because there was not enough sample. None of the enrolled patients were excluded. So, the final number of enrolled participants is 75 controls and 109 patients with the disease of interest (T1dm)

Controls and TIDM patients were comparable regarding gender, age, and BMI. 45%, and 55% females, respectively), age (8.7± 1.5, 8.2±1.5, respectively), and BMI (17±5.1, 16±4.2 kg/m^2 respectively) .

The average HbA1c for all TIDM patients (n = 109) was 9.2%, while the control group's was 5.4%. For glycemic control analysis, T1DM patients were split into two HbA1c readings in the groups: group A (HbA1c < 7.0%), group B (HbA1c > 7.0%), and group C (control). Table I displays the sociodemographic and metabolic data for the case and control groups of individuals. The study's findings indicate that there were statistically significant differences in age between groups A and C of study patients and the control group (p value = 0.036).

The uncontrolled hyperglycemia group had a higher BMI (17±2.3) than the controlled hyperglycemia and control groups (15±2.4 and 16±4.1, respectively). Group B had considerably higher HbA1c levels (9.7±2.1) compared to groups A and C (6.3±1.1 and 5.4±1, respectively). Uncontrolled hyperglycemia or group B had considerably higher fasting blood sugar levels (233±3.3) compared to groups A and C (128±5.4, 88±5.1, respectively). The lipid profile, liver enzymes, and kidney function tests showed no significant changes between the groups.

Table 1: socio-demographic and metabolic characteristics of the three groups

Variables	Group A HbA1c<7.0% n = 91	Group B HbA1c≥7.0 % n = 18	Group C (Control group) n = 75	Group A and B P-value (0.05)	Group C and A P-value (0.05)	Group C and B P-value (0.05)
Gender Male: Female:	44 (48.4%) 47 (51.6%)	7(39%) 11(61%)	30 (40%) 45(60%)	0.314	0.186	0.133
Age (years)	9.1±2.3	8.6±3.2	7.1±2.2	0.223	0.036	0.121
BMI (kg/cm²)	15±2.4	17±2.3	16±4.1	0.067	0.071	0.066
HbA1c level (%)	6.3±1.1	9.7±2.1	5.4±1	<0.001	0.551	<0.001
Fasting blood sugar (mg/dL)	128±5.4	233±3.3	88±5.1	<0.001	0.221	<0.001
Total cholesterol (mg/dL)	110±1.4	121±1	107±2.1	0.027	0.011	0.023
Triglycerides (mg/dL)	83±0.1	104±1.1	96±0.7	0.031	0.041	0.013
ALT (U/L)	12±5.4	23±4.3	14±3.2	0.273	0.829	0.123
AST (U/L)	10±6.3	15±3.7	22±4.6	0.125	0.323	0.073
Creatinine (mg/dL)	0.53±0.3	0.61±.0.1	0.57±30.1	0.225	0.425	0.325
Creatinine spot urine (mg/dL)	66±7.3	120±8.2	90±9.1	0.065	0.017	<0.001
Albumin spot urine (mg/L)	12±11	20±5.5	19±7.1	0.221	<0.001	0.323

Table 2 demonstrates the non-dietary variables in the studied groups of patients and controls. Groups of diabetic children (A and B) were higher in moderate physical activity than the control group n = 46(50.6%) and n = 7(27.8%), respectively, with significant results in favor of group B compared to group C (p = 0.001). The family history of diabetes mellitus was noticeably higher among groups A and B, 66(72.5%), and 11 (61.1%), respectively, compared with the healthy non-diabetic group 25 (20%).

Table 2: Non-dietary characteristics of the three groups

Variables	Group A HbA1c<7.0% N = 91	Group B HbA1c≥7.0 % N = 18	Group C (Control) n = 75	Group A and B P-value (0.05)	Group C and A P-value (0.05)	Group C and B P-value (0.05)
Physical activity (PA) **Moderate PA** **Very good PA**	46(50.6%) 45(49.4%)	7(27.8%) 111(72.2%)	60 (80%) 15(20%)	0.071	0.074	0.001
Family history of DM **Yes** **No**	66(72.5%) 25(27.4%)	11 (61.1%) 7 (38.9%)	25 (20%) 50(80%)	0.001	0.084	<0.001
Time length of sun exposure **Limited** **Enough**	50(54.9%) 41(45.1%)	9 (50%) 9(50%)	41.25(55%) 33.7(45%)	0.422	0.222	0.323

The relationship between vitamin D levels in type 1 diabetics and the control group is shown in Table 3. A blood vitamin D level below 20 ng/ml is considered a vitamin D insufficiency, according to the Endocrine Society. Of participants in groups A, B, and C, 62/91 (68.3%), 15/18 (83.3%), and 54/75 (72%) had vitamin D deficiency; 20/91 (21.9%), 1/18 (15.6%), and 15/75 (20%) had vitamin D insufficiency, This happens when vitamin D levels drop between 21 and 29 ng/ml; vitamin D sufficiency was found between 30 and 100 ng/ml. Because vitamin D insufficiency is common and vitamin D levels are low, the control group (n = 54, 72%) was selected. Glycemic control and vitamin D were the dependent variables. The blood levels of vitamin D were used to statistically classify each group. When compared to group A T1DM patients (p = 0.030) and group C (the controller group) (p = 0.034), cross-sectional investigations in the poor glycemic control group (group B) revealed a greater percentage of vitamin D deficiency and lower vitamin D levels. The results showed statistical significance.

Table 3. Comparison of vitamin D levels (deficiency, insufficiency, and sufficiency) between patients and control group

Vitamin D status	Group A HbA1c < 7.0% N = 91	Group B HbA1c ≥ 7.0% N = 18	Group C (Control group) N = 75	Group A and B P-value (0.05)	Group C and A P-value (0.05)	Group C and B P-value (0.05)
Deficient	62 (68.3%)	15(83.3%)	54 (72%)	0.030	0.033	0.034
Insufficient	20 (21.9%)	1 (15.6%)	15 (20%)	0.0423	0.074	0.022
Sufficient	9 (9.8%)	2 (11.1%)	6 (8%)	0.222	0.452	0.692

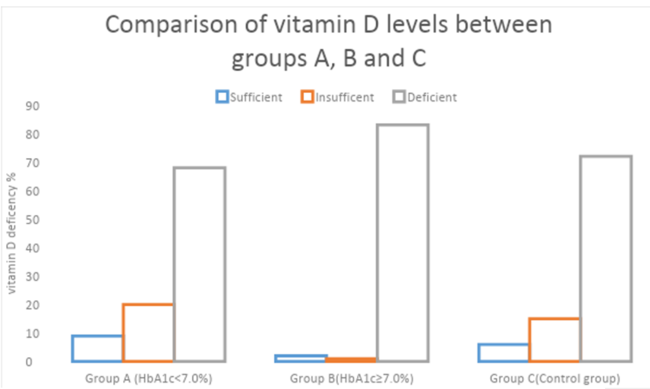

Figure 1: Comparison of vitamin D levels between groups A, B and C

Discussion

As far as we are aware, no population-based research has looked into the connection between vitamin D and type 1 diabetes in kids, or the non-dietary factors that go along with it, in Jordan. It has long been advised to use vitamin D, either in food or as a supplement [17]. There may be a connection between vitamin D insufficiency during childhood and the later onset of type 1 diabetes, according to recent studies on populations with the disease [18]. The study's findings demonstrated that children with type 1 diabetes had noticeably greater levels of vitamin D insufficiency than children without the disease. Children with type 1 diabetes and healthy children have very different mean vitamin D levels. Although vitamin D deficiency was common across all demographic groups, it was far more common in children with diabetes, particularly those whose HbA1c was greater than 7%. This result supports other studies showing that children with type 1 diabetes mellitus are more likely to have inadequate vitamin D levels. Our results showed that 77 of the 109 patients analyzed in this study had vitamin D insufficiency, which represents 77% of the patients. Eleven patients (10.1%) had adequate vitamin D levels. 25(OH)D had an average value of 26.32 5.22 mg/dL. Compared to a study conducted by 19, where the rate of vitamin D deficiency was 90.6%, the rate in this study was lower. This discrepancy could be for age sex duration of sun exposure and sunlight intensity as well as different geographical locations ranging across study sites.

One out of every two seniors (65 and older) is found to be vitamin D deficient. This proportion is significantly lower in the younger population. Every habitat has sun exposure, which stimulates outdoor exercise and leads to a lower vitamin D shortage. The amount of testosterone correlates positively with the concentration of vitamin D. This association is primarily prevalent in males. The results of one of the retrospective cohort studies revealed that male patients had a vitamin D insufficiency rate of 52.6%, while female patients had a deficiency rate of 66.9%. Male patients likewise had greater concentrations of 25(OH)D than female patients. The results are consistent with those observed in Li et al's 2018 research. A study by [19] sought to examine the connection between vitamin D levels and Type 1 Diabetes (T1DM) in children and to compare the health of those with T1DM to that of healthy persons. Additionally, it addressed vitamin D insufficiency, which has been connected to type 1 diabetes.

Compared to the non-diabetic group, the diabetes group's vitamin D levels were noticeably lower according to a study including 170 diabetics and 170 non-diabetics. Additionally, their conclusions and the current investigation's findings are rather comparable.

Conclusion

The study's findings indicate that vitamin D levels were inadequate in both the diabetic and non-diabetic groups. Patients with Type 1 diabetes (T1dm) in the low glycemic control group (with HbA1c values more than 7%) had significantly lower vitamin D levels than those in the control group. According to the evidence, vitamin D supplementation may reduce the prevalence of type 1 diabetes in infants and young children. and improve glycemic control, even if overall vitamin D supplementation intake was low among research participants.

Limitations and recommendations

For the research PTH levels, amounts of Insulin and Calcium, and PTH levels were absent. Insufficient data with too many influencing factors, such as vitamin D, and failure to exclude them all made is the key to this study. Omissions were made for complexity due to detailing factors such as diet and its impact and its thorough understanding.

This study proposes that diabetics' 25(OH) D levels be evaluated on a regular basis. Specifically, if the patient fulfills any of the following criteria: being a woman, being sedentary, being overweight or obese, having dyslipidemia, having poorly controlled hyperglycemia, or having diabetes for more than a decade. vitamin D deficiency should be viewed as a risk factor for type 2 diabetes-related conditions such as dyslipidemia, poor glucose regulation, and overweight and obesity. Research into vitamin D deficiency in people with type 2 diabetes over an extended period of time is also necessary, as is treatment for diabetic patients who simultaneously have vitamin D deficiency.

Author contributions

Renad Al Mefleh ideation, research design, major text composition, and conclusion development.

Mohammed Al Mefleh. – involvement in the article's text editing and discussion of the results produced.

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Conflict Of Interest

With regard to the research, writing, and publication of this article, the authors declare that they have no potential conflicts of interest.

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