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Original article

The Association Between Vitamin D Status and Glycemic Control in Children and Adolescents with Type 1 Diabetes

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ABSTRACT

Low vitamin D levels are common in children and adolescents with type 1 diabetes. Although a link between vitamin D status and glycemic control is suggested, the direct association with poor control is unclear. This study assessed the prevalence of low vitamin D (deficiency and insufficiency) and its relationship with HbA1c in youth with type 1 diabetes. A cross-sectional study at Benghazi Medical Center, Libya, from June to September 2018 included 63 patients (33 females, 30 males), aged 6-18 years. Data on socio-demographics, HbA1c, and vitamin D levels were collected. Vitamin D levels were categorized as deficient (<10 ng/ml), insufficient (10-19 ng/ml), or sufficient (≥20 ng/ml). Glycemic control was classified as good (HbA1c ≤ 7.5%), fair (7.6%-8.5%), or poor (≥8.6%). Analysis using SPSS version 18 showed patients had a mean age of 12 years (±3.9), BMI of 19.18 kg/m² (±3.70), diabetes duration of 4.90 years (±3.03), average HbA1c of 10.10% (±2.5), and mean vitamin D level of 17.70 ng/ml (±10.8). Deficient vitamin D was found in 27% of patients, with 36.5% insufficient and 36.5% sufficient. A weak negative correlation (r= -0.112, p=0.38) was observed between 25-hydroxyvitamin D and HbA1c. Low vitamin D levels, including deficiency and insufficiency, were prevalent in youth with type 1 diabetes. However, vitamin D status did not significantly impact glycemic control in this study.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia, it has a considerable health challenge on a global scale as it affects individuals of all ages and encompasses a diverse spectrum of diseases with distinct etiologies and clinical manifestations. Among diabetes types, type 1 diabetes mellitus (T1DM) stands out as a unique entity, distinguished by autoimmune destruction of pancreatic beta cells resulting in absolute insulin deficiency [1]. The epidemiological landscape of T1DM highlights its importance as a public health concern particularly in pediatric populations. While T1DM can manifest at any age, it most commonly presents during childhood and adolescence. Epidemiological studies have documented an escalating incidence of T1DM worldwide, with an estimated annual increase of 3-5% in the pediatric population [2]. The rising prevalence of T1DM underscores the urgent need for

effective management strategies to mitigate its impact on affected individuals and healthcare systems. Complications represent a significant challenge in the management of T1DM, contributing to substantial morbidity and mortality. Acute complications, such as diabetic ketoacidosis (DKA) and hypoglycemia, necessitate prompt recognition and intervention to prevent life-threatening outcomes. Chronic complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy, underscore the importance of long-term glycemic control in mitigating the risk of complications [3].

Achieving and maintaining optimal glycemic control is paramount in T1DM management and constitutes a cornerstone of diabetes care. Glycemic control is assessed through various parameters, with glycated hemoglobin (HbA1c) serving as the gold standard for monitoring long-term glycemic control. HbA1c reflects average blood glucose levels over a span of 2-3 months and provides valuable insights into treatment efficacy and risk stratification for diabetes-related complications [4]. Treatment of T1DM involves a comprehensive approach with various treatment modalities to achieve glycemic targets and meet individualized needs and preferences. Insulin replacement therapy through either multiple daily insulin injections or continuous subcutaneous insulin infusion with an insulin pump are the primary methods of insulin administration. In addition, coordinated supportive therapies such as lifestyle modifications of a healthy, balanced diet and regular physical activity, self-regulated blood glucose monitoring and diabetes education are actively employed to support glycemic control and improve patient quality of life [5].

Vitamin D, a fat-soluble vitamin, plays a crucial role in various physiological processes beyond its classical function in calcium homeostasis and bone metabolism. Chemically, vitamin D refers to a group of sterols, with vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) being the two major forms. Vitamin D2 is derived from plant sources, whereas vitamin D3 is primarily synthesized in the skin upon exposure to ultraviolet B (UVB) radiation. In the skin, 7-dehydrocholesterol is converted to previtamin D3, which undergoes thermal isomerization to form vitamin D3. Both forms of vitamin D undergo hydroxylation in the liver to form 25-hydroxyvitamin D [25(OH)D], the major circulating form of vitamin D, and subsequently in the kidneys to its active form, 1,25-dihydroxyvitamin D [1,25(OH)2D], which exerts biological effects through interaction with the vitamin D receptor (VDR) [6]. The primary function of vitamin D is to regulate calcium and phosphate homeostasis, essential for bone mineralization and skeletal health. Beyond its traditional role, vitamin D is implicated in diverse physiological processes, including cell proliferation, differentiation, immune regulation, and inflammation. Notably, vitamin D receptors (VDRs) are expressed in various tissues, including pancreatic beta cells, immune cells, and insulin-sensitive tissues, suggesting potential roles in glucose homeostasis and immune function.

Numerous epidemiological investigations largely point toward a strong reverse correlation between vitamin D levels and T1DM occurrences. The majority of observational studies exhibit that serum 25-hydroxy vitamin D concentrations were significantly reduced in T1DM patients compared to healthy control groups indicating a possible implication of vitamin D deficiency in mediating the autoimmune destruction of beta cells. It is believed that vitamin D is known to alter the immune system responses by enhancing T-cell regulatory functions, production, and activation of cytokines, and expression of MHC and co-stimulatory molecules [7]. In addition to its role in T1DM incidence, vitamin D status has been implicated in glycemic control in individuals with diabetes. Experimental studies have suggested that vitamin D may enhance insulin sensitivity and pancreatic beta-cell function, leading to improved glycemic control. Observational studies have reported associations between low vitamin D levels and poor glycemic control, as reflected by elevated HbA1c levels, insulin resistance, and increased risk of diabetes-related complications [8]. This study aims to explore how vitamin D level correlate with glycemic control in children and adolescents with type 1 diabetes.

METHODS

A cross-sectional study was conducted at the Pediatric and Transition Clinic of Benghazi Medical Center from June to September 2018. The study enrolled sixty-three participants, encompassing both sexes, diagnosed with well-established type 1 diabetes according to the American Diabetes Association (ADA) criteria. The age range of participants was six to eighteen years. Informed verbal and written consents were obtained from all participants, and data were collected through structured interviews to acquire demographic information, details on sun exposure, history of previous vitamin D analysis, and reasons for undergoing such testing.

Exclusion criteria encompassed patients with diabetes types other than type 1 (T1DM), individuals with known liver or kidney diseases, those using medications known to interfere with vitamin D level (e.g., antiepileptic drugs, cholestyramine, orlistate, corticosteroids), and patients who had received vitamin D supplements within the preceding nine months. Vitamin D level was categorized as deficient (<10 ng/ml), insufficient (10-19 ng/ml), and sufficient (≥20 ng/ml), while glycemic control was classified as good (HbA1c ≤ 7.5%), fair (7.6-8.5%), and poor (HbA1c ≥ 8.6%). HbA1c levels were measured using turbidimetric immunoassay via Cobas Integra 400, while vitamin D level was

assessed through electrochemiluminescence immunoassay via Cobas Integra 411. Standardized laboratory protocols were followed, and measurements were conducted by the same technicians to ensure consistency and minimize procedural variations. Data were collected, organized, tabulated, and analyzed using the Statistical Package for the Social Sciences (SPSS) version 18. Pearson correlation test was employed to assess the relationship between vitamin D status and glycated hemoglobin, with a significance level set at $p \leq 0.05$.

RESULTS

General characteristics of participants

As shown in Table 1, out of 63 participants, males represented 47.6% while females represented 52.4%. The mean age was 11 years (±9.91), with HbA1c averaging 10.10% (±2.5%), diabetes duration at 4.9 years (±3.06), vitamin D level at 17.70 ng/ml (±10.8), and BMI at 19.1 kg/m^2 (±3.7).

Table 1. General characteristics of participants

Parameters	Mean
Age (year)	11 years (±9.91)
Diabetes duration (years)	4.9 years (±3.06)
Body mass index (kg/m)	19.1 kg\m (8±3.7)
HbA1c (%)	10.10 % (±2.5%)
Vitamin D (ng\ml)	17.70 ng\ml(±10.8)

Glycemic control distribution

As shown in figure 1, that poor glycemic control group represent 68.3%., fair control was represented 22.2% while good control group represented 9.5%.

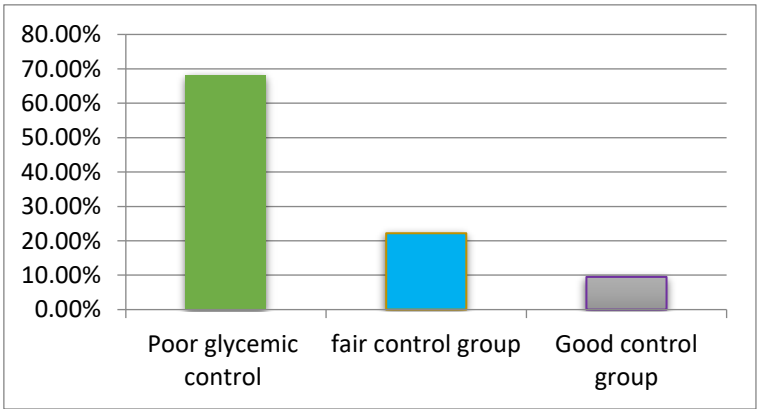

Figure 1. Distribution of glycemic control.

Prevalence of low vitamin D

Figure 2 illustrates that 63.5% of participants exhibited low vitamin D level, while 36.5% had sufficient level.

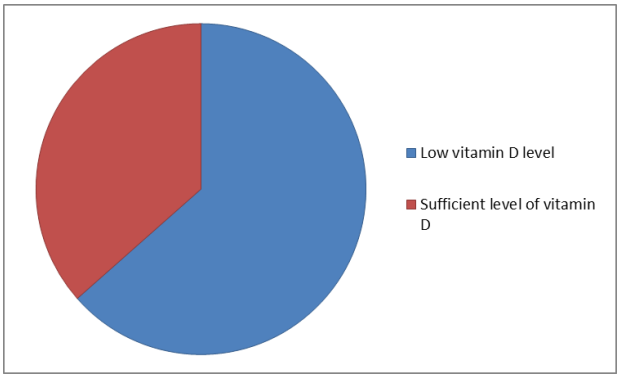

Figure 2. Distribution of low vitamin D level

Vitamin D deficiency and insufficiency

In figure 3, vitamin D deficiency was observed in 27% of participants, while 73% exhibited vitamin D insufficiency.

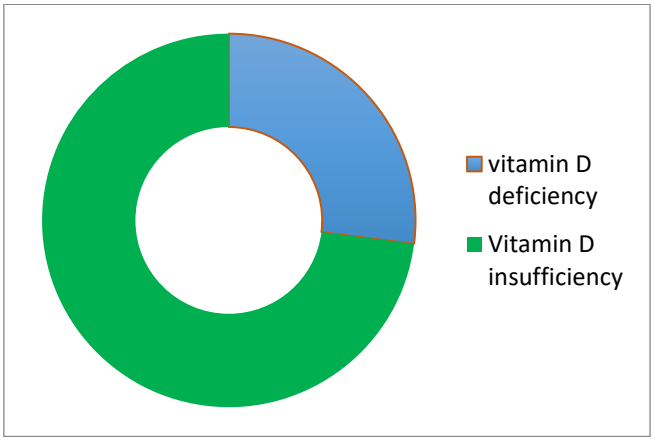

Figure 3. Vitamin D deficiency versus insufficiency

Distribution of low Vitamin D level according to gender

Figure 4 indicates a higher prevalence of low vitamin D level in females (72.7%) compared to males (53.3%).

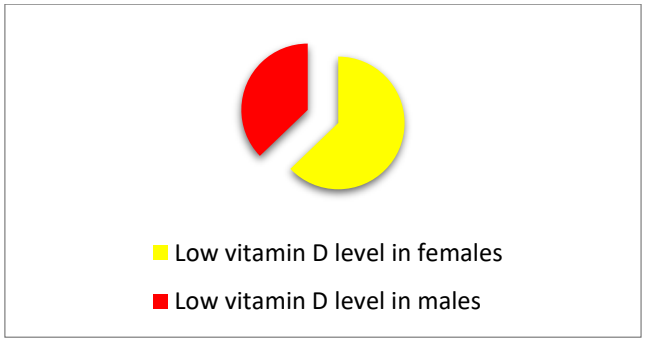

Figure 4. Low vitamin D in males versus females.

Distribution of Vitamin D Deficiency according to gender

Figure 5 highlights a greater prevalence of vitamin D deficiency in females (33.8%) compared to males (20%).

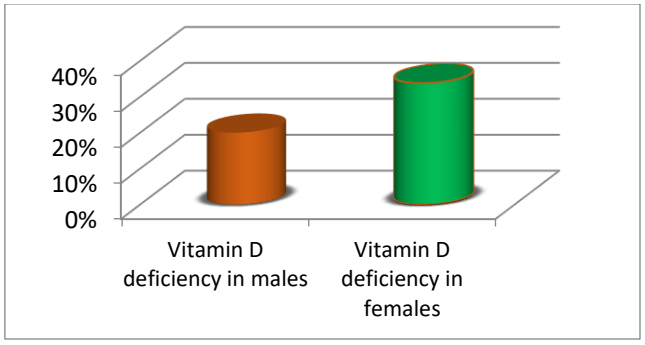

Figure 5. Vitamin D deficiency in males versus females.

Correlation between Vitamin D Status and Glycemic Control

As shown in figure 6, the analysis revealed a weak negative correlation between vitamin D status and HbA1c, with a correlation coefficient of r = -0.112 and a statistically insignificant P value of 0.38.

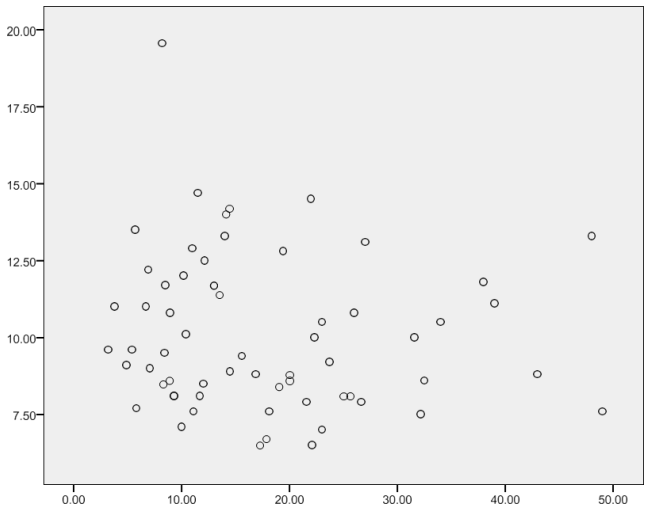

Figure 6. The association between vitamin D status and glycemic control.

DISCUSSION

The aim of this study was to determine the prevalence of low vitamin D status (deficiency and insufficiency) and investigate the potential relationship between 25-hydroxyvitamin D (the functional indicator of vitamin D status) and HbA1c (the standardized index of glycemic control) among children and adolescents with T1DM at the endocrine pediatric clinic of Benghazi Medical Center.

The glycemic control in our sample was generally poor, despite all participants being on intensive multiple insulin therapy. Only 9.5% of participants achieved good control (HbA1c ≤ 7.5%), 22.2% had fair control (HbA1c between 7.6% to 8.5%), while 68.3% exhibited poor control (HbA1c ≥ 8.6%). A consistent finding of poor glycemic control was reported by another study with 1.6% achieving good control, 22.2% having fair control, and 76.2% showing poor control [9] . In contrast, another study a study demonstrated better glycemic control, with 27.9% in the good control group, 48.2% in the fair control group, and only 22.8% in the poor control group [10]. The mean HbA1c in our sample was 10.10% (± 2.5). Males exhibited a slightly lower mean of 9.19% (±2.2), while females had a mean of 10.2% (±2.7). Our findings were consistent with a cross-sectional study conducted in Kuwait in 2016, which reported a mean HbA1c of 10.08% (±2) (9). In contrast, our mean HbA1c was higher than those reported in studies conducted in Britain and the United States, with mean values of 8.6% (±1) and 8.6% (±1.4) respectively [10,11]. Several factors may contribute to the poor glycemic control observed in our sample, including patients' lack of commitment to regular follow-up and multiple daily blood glucose monitoring required for dose adjustment, as evidenced by many patients not having glucometer strips for blood glucose monitoring. Regarding vitamin D status, the mean vitamin D level in our sample was 17.70 ng/ml (± 10.8), lower than reported in other studies of children and adolescents with type 1 diabetes. For instance, another study reported a slightly higher mean vitamin D level of 18.88 ng/ml (9) , while other studies showed even higher means, such as 21.6 ng/ml (± 2.2) and 21.8 ng/ml (±17)[12,11]. Low vitamin D status (≤ 20 ng/ml) was markedly prevalent in our sample, with 63.5% affected, particularly dominant in females. Our findings were higher than those reported by another study where low vitamin D level represented 48.6% (11), but lower than studies reporting percentages of 77% and even 90% (13,12). Despite most participants not having risk factors such as obesity, autoimmune diseases, or dark skin pigmentation, low vitamin D status may be related to poor sun exposure, particularly among females. In our sample, 27% had vitamin D deficiency (< 10 ng/ml), lower than percentages reported in other studies, which reached up to 60% (10,12). However, a British study reported a lower percentage of vitamin D deficiency at 8.4% (11). The percentage of vitamin D insufficiency (10-19 ng/ml) in our study was 73%, similar to other studies but higher than that found in a study of Kuwaiti patients (19%) (9). This lower percentage of vitamin D deficiency in our study compared to others may be attributed to seasonal variation. Our study, conducted from June to September, contrasts with other studies conducted in different months. Furthermore, differences in participant ethnicity may have influenced vitamin D levels. In our study, females had a higher percentage of vitamin D deficiency and insufficiency compared to males, possibly due to poorer sun exposure among females. This finding is consistent with another study where females had a higher percentage of vitamin D deficiency and insufficiency [13]. Interestingly, participants previously screened for vitamin D and on vitamin D treatment had lower vitamin D levels compared to those not screened, possibly due to corresponding factors such as poor sun exposure and diet.

Regarding the association between vitamin D status and glycemic control, our study found a very weak negative

correlation between vitamin D status and HbA1c, with an insignificant P value (r= -0.112 and P=0.38). This finding is consistent with that of a study in the diabetic center at the Children's Hospital of Philadelphia, which found no association between vitamin D status and glycemic control marker [10]. Similarly, our finding aligns with another study which reported no significant correlation between vitamin D status and glycemic control in 348 diabetic patients [11]. In contrast, other studies have shown a significant correlation between vitamin D status and glycemic control, such as that conducted in Kuwait (r=-0.374, P=0.003) p [9] and a study in Saiful Anwar Hospital in Indonesia (r= -0.878, P=0.000) [12].

CONCLUSION

Our study found that despite the prevalence of low vitamin D level among children and adolescents with type 1 diabetes, vitamin D status did not significantly influence glycemic control. This suggests that factors other than vitamin D may be more influential in managing blood sugar levels in this population.

Acknowledgments

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Conflicts of Interest

The authors declare no conflicts of interest.

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العلاقة بين مستوي فيتامين د والتحكم في السكر لدى الأطفال والمراهقين المصابين بداء السكري من النوع الأول

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المستخلص

ينتشر انخفاض مستوى فيتامين د بين الأطفال والمراهقين المصابين بداء السكري من النوع الأول. على الرغم من تراكم الأدلة التي تدعم وجود علاقة بين حالة فيتامين د والسيطرة على نسبة السكر في الدم لدى مرضى السكري، لا يزال من غير الواضح ما إذا كان انخفاض مستوى فيتامين د مرتبطًا مباشرة بسوء السيطرة على نسبة السكر في الدم في هذه الفئة من المرضى. هدفت هذه الدراسة إلى تقييم انتشار انخفاض حالة فيتامين د بين مرضى السكري من النوع الاول من الاطفال والمراهقين والتحقيق في العلاقة المحتملة بين 25-هيدروكسي فيتامين د (مؤشر وظيفي لحالة فيتامين د) والقدرة علي التحكم في السكري . أُجريت هذه الدراسة المقطعية في عيادة الأطفال بمركز بنغازي الطبي، بنغازي-ليبيا، بين يونيو وسبتمبر 2018. شملت الدراسة ثلاثة وستين طفلاً ومراهقًا مصابين بداء السكري من النوع الأول (33 أنثى، 30 ذكرًا) تتراوح أعمارهم بين 6 إلى 18 عامًا. تم جمع البيانات الاجتماعية والديموغرافية ومستوي فيتامين د ومعدل السكر التراكمي للمرضي حيث اعتبر مستوي فيتامين د < 10 نانو جرام/مل نقصا والمستوي بين م 10-19 نانو جرام/مل كمستوي غير كافي و ≥20 نانوجرام/مل كمستوي الكفاية. تم تصنيف التحكم في مستوى الجلوكوز في الدم إلى ثلاث فئات: جيد (قيمة ≥ 7.5%)، متوسط (7.6%-8.5%)، أو ضعيف (≤8.6%). تم جمع البيانات وادخالها وتحليلها احصائيا. كان متوسط عمر المرضى 12 عامًا (±3.9)، ومؤشر كتلة الجسم 19.18 كجم/م² (±3.70)، ومدة الإصابة بالسكري 4.90 سنوات (±3.03). كان متوسط مؤشر التحكم بالسكر التراكمي 10.10% (±2.5)، ومتوسط مستوى فيتامين د 17.70 نانوجرام/مل (±10.8). تم العثور على نقص فيتامين د في 27% من المرضى، و36.5% كانت لديهم مستويات غير كافية، بينما كانت مستويات الفيتامين كافية في 36.5% من المشاركين . لوحظت علاقة سلبية ضعيفة بين 25-هيدروكسي فيتامين د ومؤشر التحكم بالسكر التراكمي. بشكل عام، كانت مستويات فيتامين د المنخفضة، بما في ذلك النقص وعدم الكفاية، منتشرة بين الاطفال والمراهقين المصابين بالسكري من النوع الاول. ومع ذلك، لم يكن لحالة فيتامين د تأثير كبير على التحكم في مستوى السكري في الدم في هذه الدراسة.

الكلمات الدالة. السكري من النوع الاول, معدل السكر التراكمي, التحكم بمستويات السكري, فيتامين د.