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Effect of Vitamin D Supplementation on Glycemic Control in Children with Type 1 Diabetes Mellitus: A Randomized Clinical Trial

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Abstract **Background:** Vitamin D endocrine system is a potential immune system modulator and has been implicated in the pathogenesis of several autoimmune diseases including type 1 diabetes mellitus. A relationship between type 1 diabetes and vitamin D deficiency has been reported, in which low vitamin D levels are shown to have a negative effect on beta-cell function. **The aims** of the study were to investigate vitamin D status and to evaluate the effect of vitamin D3 supplementation on glycemic control in children with type 1 diabetes. **Method:** A randomized clinical trial including 80 children who were newly diagnosed with type 1 diabetes and randomly assigned into either control or intervention arm was used. Vitamin D status and Glycohemoglobin (HbA1c) were assessed initially for both the study two arms. Diabetic children of the intervention arm who had vitamin D deficiency and insufficiency were treated with 4000 units of vitamin D3 and calcium (500 mg/day) in oral liquid form. After the study interference (3 months later), HbA1C was measured again for both arms as an indicator for glycemic control. Differences in mean±SD HbA1C and body mass index were assessed before and after the study. **Results:** The mean of body mass index in intervention arm was 14.77±3.49, while in control arm was 17.84±3.87, with statistically significant deference between two arms P<.001. Furthermore, the mean change in HbA1c levels in intervention arm was 6.78±1.94 compared with 7.03±1.83 in control arm, with no statistically significant deference detected between children of the study two arms P<.460. **Conclusion:** Vitamin D3 supplement on the clinical base improves glycemic control in pediatrics with type I diabetes mellitus and vitamin D deficiency.

Keywords: *Vitamin D, Glycemic control, Children, Type 1 diabetes mellitus, Glycohemoglobin (HbA1c)*

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1. Introduction

Type 1 diabetes mellitus (T1DM) is an immune-mediated disease characterized by diminished insulin secretion due to damage to islets of Langerhans in the pancreas, which eventually results in high levels of glucose in the blood. [1] Approximately, 90% of diabetes in children and adolescents is of type 1. [2] High prevalence of hypovitaminosis D in children and adolescents with T1DM has been reported in several epidemiological studies suggesting that, children with T1DM have a predisposition towards vitamin D deficiency as compared to healthy peers. [3,4,5,6,7] The sun is the primary source of vitamin D, which is synthesized endogenously in skin to produce cholecalciferol (vitamin D3), although less than 10% of vitamin D comes through diet from a limited range of foods such as milk and other calcium-containing foods. [8,9] The main marker of vitamin D status is the metabolite 25-hydroxyvitamin D [25(OH)D], which is synthesized in the liver.

In recent years, the extra-skeletal effects of vitamin D (25OHD) have raised considerable interest since specific receptors has been found in many tissues and systems, including pancreatic β cells and immune cells. [10] The prevalence of vitamin D deficiency in children with type 1 diabetes is ranged from 15% to 90.6%. [11] Emerging studies have demonstrated an inverse risk relationship between T1DM and vitamin D levels, and also shown a reduced risk of the disease with its supplementation. [7,12,24] There are evidences that regular doses of vitamin D early in life have been shown to reduce the risk of developing T1DM by 29% [13], and vitamin D is important in the prevention of islet cell death, and it improves the production of insulin. Moreover, vitamin D treatment has also been investigated to improve glycemic control through enhancing insulin sensitivity in 60% of

pediatric patients with type 1 diabetes. These effects have been mainly attributed to the immuno-modulatory actions of vitamin D. [14,15]

A recent meta-analysis of case-control studies showed 25OHD levels were lower than 5.69 ng/ml in children with T1DM compared with healthy controls. [16] This reduction seems to be higher in subjects with diabetic ketoacidosis. [4] Another two studies involved children and adolescents presented that, low levels of vitamin D have been associated with insulin resistance in children with type 1 diabetes, and those at risk for diabetes and vitamin D and calcium supplementation improved glycemic control in a 12-week. [12,17] In addition, it seems that low 25OHD levels produce an inflammatory status in pancreatic islets, leading to disequilibrium in insulin sensibility and secretion, with consequently insulin resistance and T2DM, which nowadays affects 10% of children population. [18,21] Moreover, vitamin D seems to affect glucose homeostasis via a direct effect on β cells and an indirect effect through calcium regulation, since insulin secretion is calcium-dependent. [10,19]

1.1. Problem Statement

However, the impact of 25OHD status on metabolic control is debated with no sufficient evidence to recommend screening children who are at risk for vitamin D deficiency or to prescribe vitamin D supplementation to attain the benefits of glycemic control for subjects with type 1 diabetes mellitus is still unclear [12,15,20].

1.2. Aim

This study was aimed to investigate vitamin D status and to evaluate the effect of vitamin D3 supplementation on glycemic control in children with type 1 diabetes mellitus.

Outcome measures

The primary outcome was to assess the mean difference in glycohemoglobin (HbA1c) levels of diabetic children; however **the secondary outcome** was to assess the mean difference in body mass index of diabetic children in both the study two arms over the study intervention period (three months).

1.3. Research Hypothesis

It is hypothesized that: vitamin D3 supplementation may improve glycemic control in children with type 1 diabetes mellitus who are vitamin D deficient, and insufficient.

2. Subjects

2.1. Study Design

A randomized clinical trial was used.

2.2. Setting

The study was conducted at endocrinology outpatients' clinic - Children Hospital affiliated to Mansoura University, a tertiary care teaching hospital.

2.3. Study Sample

Children who were newly diagnosed with type 1 diabetes mellitus and had vitamin D deficiency, or insufficiency, which indicated by its levels of less than 20 ng/ml or 21–29 ng/ml respectively [22] were recruited in this study.

Data were collected throughout 6 months, started from September 2018 to March 2019. In this period, 80 children who were above 2 years old, and recently determined through two fasting blood glucose level greater than 126 mg/dl or HbA1c cut point of ≥6.5% as diabetic patients [23], and those who presented to the pediatric intensive care unit with diabetic ketoacidosis (DKA) at first time were included. Children with hepatic or renal problem s or those who receive any drug therapy that may affect vitamin D (VD) metabolism were excluded from the study sample. All children enrolled in the study were followed up during their regular screening visits to endocrinology outpatient's clinic to assess glycemic control, and especially children of the intervention arm were assessed for the side effects of VD supplementation if any.

Sampling

A cluster random sampling technique was applied to assign children with the previously mentioned criteria into intervention and control arms. Cluster was classified based on day of attendance to the study setting (outpatients' clinic). Flip of a coin was used as a first step to determine day of intervention arm and day for control arm. Head (Saturday) assigned to intervention arm and tail (Tuesday) was assigned to control arm, until the required sample size was completed.

For sample size calculation, a similar study from Saudi Arabia [24] showed that, vitamin D supplementation for 12 weeks reduced HbA1c by 10% with a standard deviation of 2.4. It was estimated that at least 24 children in each arm (intervention or control) would be required to achieve 80% power; α=0.05 and two sided 95% CI to detect a mean difference of 2 % in HbA1c between the study two arms.

Power analysis

Usage of Medcalc software, with a 95% confidence interval and 80% power of test revealed that, 74 children at least (37 in both intervention and control arms) were required to test the current study hypothesis. This number was increased to 80 children (42 in intervention arm and 38 in control arm) to overcome dropout.

2.4. Tools of Data Collection

Data were collected by using children's health assessment structure interview sheet. It was developed by the researchers based upon relevant literature. This tool was consisted of three parts:

Part I: Children's socio-demographic characteristics

This part was aimed to collect socio-demographic characteristics for both intervention, and control arms before the intervention such as: age, sex, birth order and level of education.

Part II: Children's current health history

It was used to assess children's weight, height and body mass index (BMI). It also covered the prescribed treatment for T1DM, including the total daily requirement of insulin (units/Kg/day), and type of insulin. This part had been used before the intervention for both the intervention, and control arms.

Part III: Children's laboratory investigations

This part of the tool addressed HbA1c that was investigated and recorded before, and after the interference for both intervention, and control arms. Additionally, vitamin D status was assessed and recorded before the intervention for both intervention, and control arms.

3. Method

Preparation phase

- It was started with the administrative process, in which an official letter was issued from the Faculty of Nursing; Mansoura University to the director of endocrinology outpatients' clinic-Children Hospital to permit the researchers to carry out the study.
- The tool of data collection was developed by the researchers after thorough review of the current related literature.
- The developed tool was tested for its validity and reliability. The content validity of the tool was assessed by 5 experts in the field of pediatric nursing, community health nursing, and pediatric medicine. Recommended modifications were made accordingly. Moreover, the tool reliability was tested by using Cronbach's alpha test (α= .86).

Ethical consideration

The study proposal was approved by the Research Ethics Committee of Faculty of Nursing, Mansoura University. The legal guardians (parents) of the participants' children and older children who were 7 years old or above were informed about the aims, procedure, expected outcomes, and potential risks of the study. They were assured that allowing their children to participate in the study is voluntary, and if they refused, this would not affect the health care services they received. They have the rights to ask any question and, withdraw at any time from the study without giving any reason. Legal guardians were also assured that their children's personal data would be kept confidential, and the results would not be directly linked to the children's personal data. Parents and older children were given simple explanation about the stages of the study. An informed consent was obtained from the legal guardians conveyed that they accept to allow their children to participate in the study. An assent was obtained from older children who accept to take part in the study. Safety monitoring was applied in this study. All children were followed up in the endocrinology outpatients' clinic monthly for a total duration of 3 months to detect any adverse effects, especially for the children in intervention arm who were monitored for signs and symptoms of vitamin D toxicity (vomiting, polyuria and gastritis) by a qualified pediatrician (third investigator). If any adverse effect appears, the child was immediately admitted into the Children Hospital and received immediate treatment and care. In this case, the primary investigator was provided a report to the Research Ethics Committee within 24 hours of the occurrence of the adverse event.

Exploratory phase

Pilot study

Face validity of the developed tool was tested by applying a pilot study on 10% (8 children) of the study sample who were included within the participants for cost benefit effect (the laboratory investigations were very expensive). The aim of the pilot study was to test the clarity and the applicability of the data collection tool. There were no modifications required to be done.

Operational phase/fieldwork

This randomized controlled trial was conducted in the study setting, and during the study period that previously mentioned. Due approval from the Research Ethics Committee of Faculty of Nursing, Mansoura University was obtained, accordingly informed consent from the children's legal guardians who their children were newly diagnosed with T1DM was signed. Inclusion of children in the study started with a confirmation that the child has type 1 diabetes based on elevated two fasting blood glucose level (>126 mg/dl) or HbA1c cut point of ≥6.5%, or when the child presented to the pediatric intensive care unit with the manifestations of diabetic ketoacidosis for the first time. The same inclusion and exclusion criteria were applied to assign diabetic children in the study two arms; intervention (n=42) and control (n=38). Data about socio-demographic characteristics, current health history, and body mass index of the participants were collected, and accordingly, the dose of insulin therapy including daily requirement were estimated for all children. The intervention arm was received oral calcium supplementation in a dose of 500 mg/day in addition to vitamin D3 (cholecalciferol) in a dose of 4000 IU oral liquid once a day for 3 months in addition to insulin. On the other hand, only insulin was prescribed for children of the control arm. The primary outcome variable was the mean difference in HbA1c levels after 3 months from the interference. Vitamin D dosage was calculated using upper limit of VD intake as per Practical Guidelines for the Supplementation of Vitamin D and the Treatment of Deficits in Central Europe, 2013 and Endocrine Society clinical practice guideline, 2011. [25,26] Laboratory investigations in the form of plasma HbA1c, and serum 25-OHD were measured at baseline, and then HbA1c repeated after 3 months. The compliance to vitamin D and calcium supplementation were recorded.

Legal guardians and older children of both arms were counseled regarding importance of compliance to the treatment regimen at home. A free glucometer was issued to each child, along with a diabetic diet chart and a diabetes information handout for the parents or diabetic children according to their level of understanding. Insulin doses were titrated by a Pediatric Endocrinologist who was involved in the study. All children followed up throughout the study period. Legal guardians were contacted over phone if the monthly follow up date was missed.

Data collection technique

- The researchers were attended the endocrinology outpatients' clinic for 2 days/week (Saturday and Tuesday). These two days were allocated for diabetic children's diagnosis and their follow-up visits.
- At the beginning of the interview, the researchers were communicated with the children's legal guardian(s), introduced themselves and provided simple, comprehensive information about the study. If any of the child's parents refused to allow her/his child to participate in the study, another participant was selected.
- Diabetic children were randomly assigned either to an intervention arm (who received vitamin D3 and calcium supplementation orally) and a control arm (who received standard of care).
- The researchers were collected and recorded the required data from eligible children or their guardians, using health assessment structure interview sheet. The pre-planned laboratory investigations were done in CAP accredited medical lab at the expense of the researchers for both the study two arms.
- A pediatrician, (a member of the research team) who has a PhD degree, and is working at the Pediatric Endocrinology and Diabetes Unit was responsible for estimating and describing the doses of vitamin D and calcium supplementation. Moreover, many instructions were given to the legal guardians of the participants' children in both the study two arms to control blood sugar spikes with diet, insulin administration, as well as exercise.
- Concerning the laboratory investigations; vitamin D status was assessed by measuring the concentration of 25-hydroxyvitamin D [25(OH)D] in the children's serum. Levels of 25(OH)D were interpreted as deficiency (≤20 ng/ml or ≤50 nmol/L), insufficiency (21–29 ng/ml or 52.5-72.5 nmol/L), and sufficiency (30-100 ng/ml ng/ml or 75-250 nmol/L). The glycohemoglobin levels are defined based on the control of diabetes, as good control (HbA1C<7.8%), fair control (HbA1C:7.8%-9.9%), and poor control (HbA1C>9.9%). [27]

Statistical analysis

Data were analyzed using SPSS (Standard for Statistical Product and Service Solutions) version 24 to obtain the results and differentiate between the study two arms. Quantitative data like 25-OHD levels, HbA1c, insulin dose/day were represented using mean±SD. Comparison of quantitative data over the study time 2 points between the study two arms were done using a paired t-test. A p-value <0.05 was considered significant.

4. Results

Table 1 showed the homogeneous matching in baseline characteristics, metabolic parameters and differences at time zero in both intervention and control arms. This is obvious in the ratio between female to male that was 22: 20 in intervention arm and 20: 18 in control arm, there was no statistically significant deference between two arms P=.982. Child's birth order was first, second and third representing 35.7%, 40.5% and 23.8% in intervention arm and 44.7%, 36.8% and 18.4% in control arm respectively, there was no statistically significant deference between two arms P=.688. Elementary level of education was 71.4% and 76.3% in both intervention and control arms respectively, there was no statistically significant deference between two arms P=.642.

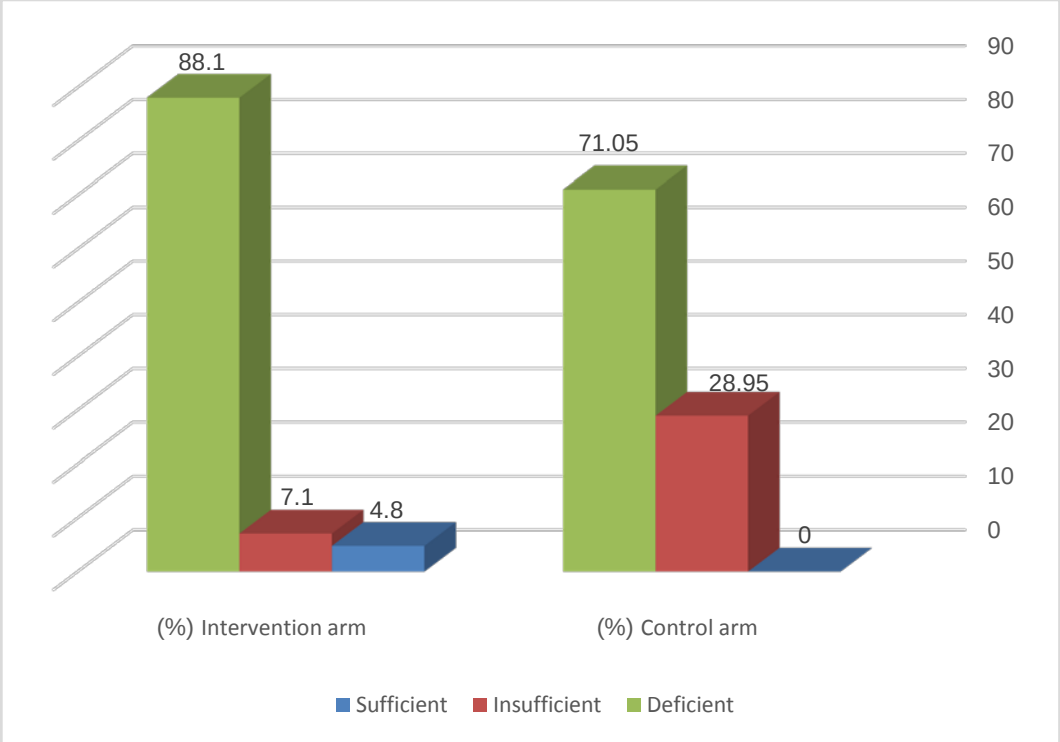

Figure 1. Percentage distribution of vitamin D status in both the intervention and control arms at T0 (n=80)

In relation to mean age, it was found 8.40±3.32 and 8.87±3.13 years old in both intervention and control arms respectively, there was no statistically significant deference between two arms P=.522. Body mass index means in both intervention and control arms were 17.11±3.99 and 18.61±4.00 respectively, there was no statistically significant deference between two arms P=.095. Mean of diagnostic HbA1c levels was 10.62±1.69 and 11.09±1.72 in both intervention and control arms respectively, there was no statistically significant deference between two arms P=.222. Mean of metabolite 25-hydroxyvitamin D levels in both intervention and control arms was 15.59±6.96 and 15.57±5.75 ng/ml respectively, there was no statistically significant deference between two arm P=.992. Mean of insulin requirement was 0.930±0.325 and 0.869±0.303 IU/kg/day in both intervention and control arms respectively, there was no statistically significant deference between two arm P=.384. Finally, doses of vitamin D supplementation and calcium were 4000 IU/day and 500 mg/day respectively for intervention arm only.

On the other hand, Table 1 at time one (after 3 months) clarified that 92.86% of intervention arm were kept on taking calcium (Ca+) and vitamin D supplementations. The mean difference of BMI of intervention arm was 14.77±3.49, while in control arm was 17.84±3.87, with statistically significant deference between two arms P<.001. Furthermore, the mean difference of HbA1c in intervention arm was 6.78±1.94, while in control arm was 7.03±1.83, with no statistically significant deference detected between children in the two arms P<.460.

Table 2 and Figure 1 declared that 88.10% of children in intervention arm had vitamin D deficiency compared to 71.05% in the control arm at time zero. There was no statistically significant deference between the study two arms P= .403.

Table 3 and Figure 2 illustrated that 88.10% of intervention arm had good control over HbA1C level compared to 76.32% in the control arm at time one. There was no statistically significant deference between the study two arms P= .493.

Table 1. Baseline characteristics, metabolic parameters and differences in both the intervention and control arms at the onset of T1DM diagnosis (T0) and 3 months later (T1) [n=80]

Variable	All	Intervention arm	Control arm	Test of Sig.
T0 (at the onset of T1DM diagnosis)				
Number (%)	80 (100)	42 (52.5)	38 (47.5)	
Mean age (ys)±SD	8.62±3.22	8.40±3.32	8.87±3.13	t= .643 P= .522
Female : Male	42: 38	22: 20	20: 18	X^2= .001 P= .982
Child's birth order, No. (%)	First	15 (35.7)	17 (44.7)	X^2= .747 P= .688
	Second	17 (40.5%)	14 (36.8)	
	Third	10 (23.8)	7 (18.4)	
Child's level of education, No. (%)	Below age	3 (7.1)	4 (10.5)	X^2= 2.516 P= .642
	Kindergarten	8(19.0)	5 (13.2)	
	Elementary	30 (71.4)	29 (76.3)	
	Secondary	1 (2.4)	0 (0.0)	
Mean weight±SD	32.01±15.25	29.47±13.77	34.82±16.47	t=1.566 P= .122
Mean height±SD	130.34±19.67	128.25±18.01	132.66±21.37	t= .992 P= .324
Mean BMI±SD	17.82±4.04	17.11±3.99	18.61±4.00	t= 1.688 P= .095
Mean diagnostic HbA1c levels (%)±SD	10.85±1.71	10.62±1.69	11.09±1.72	t= 1.232 P= .222
Mean 25(OH)D levels (ng/ml) ±SD	15.58±6.37	15.59±6.96	15.57±5.75	t= .011 P= .992
Mean insulin requirement (IU/kg/day) ±SD	0.901±0.314	0.930±0.325	0.869±0.303	t= .876 P= .384
Dose of Vitamin D supplementation (IU/day)	4000	4000	-	-
Dose of Calcium (mg/day)	500	500	-	-
T1 (after 3 months)				
Number (%)	80 (100)	42 (52.5)	38 (47.5)	-
Mean weight±SD	29.36±14.19	25.60±11.91	33.51±15.46	t= 2.542 P= .013
Mean height±SD	130.91±19.63	125.88±18.02	133.24±21.26	t= 1.002 P= .320
Mean difference of BMI±SD	16.23±3.96	14.77±3.49	17.84±3.87	t= 3.712 P<.001
Compliance to Ca+ and Vitamin D supplementation (%)	92.86%	92.86%	-	-
Mean difference of HbA1c levels (%)±SD	6.90±1.88	6.78±1.94	7.03±1.83	t= .747 P= <.460

BMI, body mass index; SDS, standard deviation score. *p < 0.05.

Table 2. Vitamin D status in both the intervention and control arms at T0 (n=80)

Vitamin D status	Intervention arm (%)	Control arm (%)	Test of Significance
Deficient	88.10	71.05	
Insufficient	7.10	28.95	X^2= 75.322 P= .403
Sufficient	4.80	0.0	

Table 3. Hemoglobin A1c levels in both the intervention and control arms at T1 (n=80)

HbA1C levels	Intervention arm (%)	Control arm (%)	Test of Significance
Good control	88.10	76.32	
Fair control	11.90	10.53	X^2= 38.496 P= .493
Poor control	7.10	13.15	

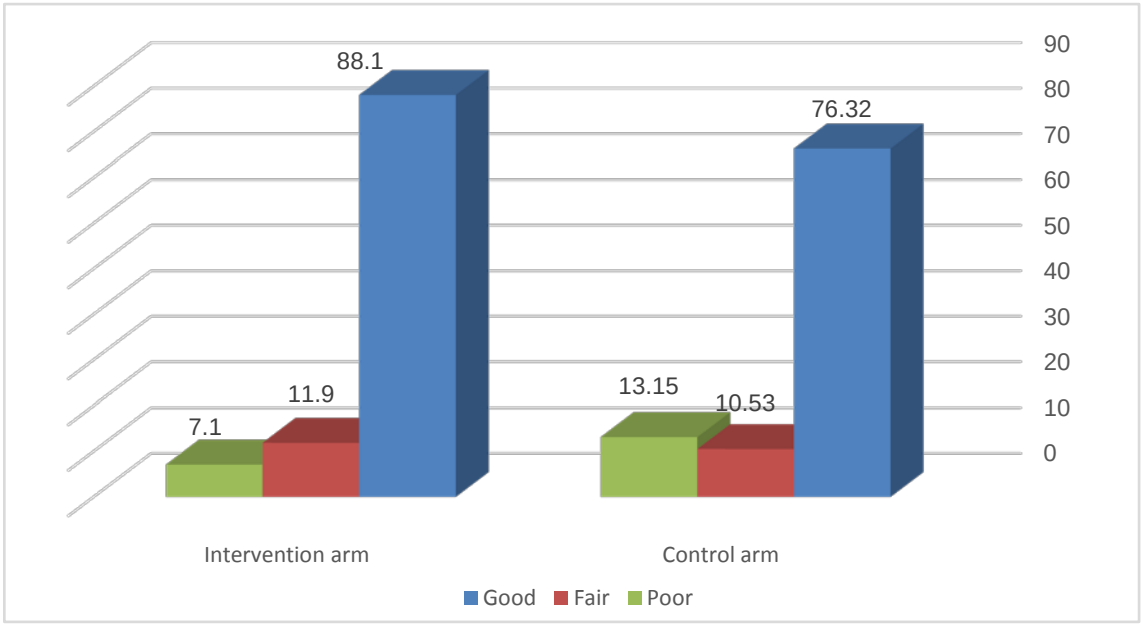

Figure 2. Percentage distribution of HbA1c levels in both the intervention and control arms at T1 (n=80)

5. Discussion

Several observational studies, randomized clinical trials (RCTs), and meta-analyses [28,29] have been conducted to investigate the effect of vitamin D supplementation on glycemic measures and insulin sensitivity in children with T1DM. Evidence indicates that vitamin D treatment improves glucose tolerance and insulin resistance [30,31]. Nevertheless the potential benefits of vitamin D supplementation on glycemic control are still debated; accordingly the current study was a trial to participate in this argument. The study was conducted on a homogeneous sample, who were matched in age, sex and means of BMI, HbA1c, 25(OH)D and insulin requirement at start point (time zero) in both intervention and control arms.

Children in the present study were above 2 years of age with mean age of 8.40±3.32 and 8.87±3.13 years old and female to male ratio was 22: 20 in intervention arm and 20: 18 in control arm. In a cohort study using The Health Improvement Network (THIN) primary care database, which contains anonymised electronic health records of >11 million patients from 639 UK general practices, mentioned that, English children was a 15-fold increase in the diagnosis of vitamin D deficiency between 2008-2013. Socio-demographic factors independently associated with higher rates of diagnosis included; older children, female sex in children aged ≥10 years old, and male sex in children aged <5 years old. [32] Developed countries were concerned with this issue many decades ago, and recently vitamin D deficiency and insufficiency become a growing public health concern among Egyptians, as it became notable among children and its consequences on their general health status.

Findings of the present study showed that mean of insulin requirement was nearly similar; 0.930±0.325 and 0.869±0.303 IU/kg/day in both intervention and control arms respectively, accordingly the majority of intervention arm and slightly more than three fourths in control arm had good glycemic control after 3 months of the onset of diabetes, as indicated by HbA1C levels. As well Savastio et al. (2006) in a cross sectional study was carried out from 2008–2014 on 141 children and adolescents with type 1 diabetes mellitus illustrated that, at time zero, the 25OHD levels were inversely related to the severity of hyperglycemia. In their study at time one and time two, subjects with vitamin D deficiency (25OHD≤25nmol/L) showed higher daily insulin requirement and HbA1c values than others vitamin D status. The 25OHD levels were negatively related with HbA1c ($p<0.001$) and daily insulin dose ($p<0.05$) during follow up [10].

In the current study at time zero, mean levels of diagnostic HbA1c was 10.62±1.69 and 11.09±1.72 in both intervention and control arms respectively and most of children in both arms had vitamin D deficiency and

insufficiency. While at time one (after 3 months) HbA1c mean in intervention arm was 6.78±1.94 compared with 7.03±1.83 in control arm. These findings were in the same line with Mohr, Garland, Gorham; Garland (2008) in their study on children aged <14 years during 1990--1994 in 51 regions worldwide observed that, there was greater incidence of type 1 diabetes with lower levels of vitamin D. [33] As well Hypponen, Laara, Reunanen; Jarvelin (2001) in a cohort study in Oulu and Lapland, northern Finland, on 10,821 children during their first year of life found that children who took 2,000 IU of vitamin D daily were 80% less likely to develop type 1 diabetes. [34] According to the present study, although there was no statistically significant deference between children received vitamin D and calcium supplementations and those who were not received them as regarding glycemic control, the result was clinically significant.

Furthermore a recent study in Egypt concluded that supplementation of vitamin D for 3 months in vitamin D deficient T1DM patients revealed that better glycemic control was achieved, albeit no reduction in insulin requirement. [7] Another study from Iran illustrated that after receiving a mega dose of vitamin D3 intramuscularly; vitamin D deficient T1DM patients lowered their mean of HbA1c. [27]

The present study declared no statistically significant difference in mean of BMI between the study two arms; intervention and control at the study start point, which converted to statistically significant difference after interference or after 3 months of vitamin D and calcium supplementation for diabetic children in the intervention arm. This was supported by Kumaratne, Early; Cisneros (2017) in a retrospective chart study about "Vitamin D deficiency and association with body mass index and lipid levels in Hispanic American Adolescents" that was carried out from February 2016 to August 2017 at a pediatric clinic in California on 264 adolescents aged 13 to 19 years. Their results presented that overweight and obese adolescents comprised 55.6% of the study sample and 33.9% of them were vitamin D deficient. The overweight or obese subjects in this sample were twice as likely to be vitamin D deficient as the underweight or healthy weight subjects [35]. This may be interpreted in the context of the fact that vitamin D insufficiency and excessive fat accumulation have mutually negative effects (i.e., the adipose tissue has an influence on the metabolism of vitamin D on the one hand, and its pathogenic role in the obesity development mechanisms on the other hand). Therefore, vitamin D and calcium supplementation improve this mutually dependent process leading to reduce body weight which reflected on the body mass index [36].

Bizzarri's study was not confirmed the protective effect of vitamin D supplementation on β cells function in recent onset diabetes. [37] Like that study, the treatment response of children with vitamin D deficiency and insufficiency in our results did not show significant difference with regard to diabetes control among children who received the study interference and their controls who did not receive (p-value= .493). From the researchers point of view the most important issues in diabetes control are to correctly calculate insulin requirement and to accurately comply with the treatment, diet and exercise regimens.

Limitations of the study

Our study was limited by number due to the high price of laboratory investigations, which also did not enable researchers to reinvestigate the status of 25-hydroxyvitamin D in the participants' serum after 3 months.

6. Conclusion

A high incidence of vitamin D deficiency and insufficiency was found among Egyptian children with T1D in both the intervention and control arms. After 3 months of oral vitamin D3 and calcium supplementation, children with type 1 diabetes mellitus belonged to the intervention arm a little bit had better glycemic control than their control, as reflected by HbA1c mean difference levels, with no statistical significant difference detected between the study two arms. However, statistically insignificant difference in children's mean BMI between the intervention arm and control arms at time zero was converted at time one to be statistically significant difference.

Approach for Further Studies

Another study to follow the pediatric patients with T1DM aims to investigate the impact of vitamin D supplementation on a possible change in insulin daily requirement dose is needed.

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Conflicts of Interest Disclosure

The authors declare no conflict of interest.

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