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Original article

Role of Hypovitaminosis D in Diabetes-Related Anemia of Chronic Disease and Value of Its Replacement in Response to Therapy: A Randomized Control Trial

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Abstract:

Background: Deficiency of vitamin D has become a global public health problem, with nearly 1 billion people worldwide being in a state of vitamin D insufficiency or deficiency. The aim of this work was to evaluate the role of hypovitaminosis D in diabetes- related anemia of chronic disease and value of its replacement in response to therapy. **Methods:** This randomized control trial included patients with diabetes- related anemia of chronic disease), the least number is 318 patients. The three groups were randomized equally; group 1 was with diabetes- related anemia of chronic disease) with normal 25 hydroxy vitamin D and received treatment for anemia, group 2 was with diabetes-related anemia of chronic disease with low level of 25 hydroxy vitamin D, and group 3 was with diabetes, but no anemia then follows up for hemoglobin concentration. Those Patients were informed about using vitamin D in treatment (benefits and side effects) in addition to treatment of specific anemia, then we assessed anemia after three months. **Results:** The study found no significant difference in age, sex, or type of diabetes mellitus (DM) between groups. However, individuals with anemia, particularly those with low vitamin D levels, had lower serum iron and TIBC levels and higher ferritin levels. Vitamin D levels were negatively correlated with ferritin and positively correlated with iron and TIBC. HbA1C levels had negative correlations with iron, TIBC, and WBCs. **Conclusion:** The current study suggested that there was close relationship between vitamin D deficiency and anemia in diabetic patients.

Keywords: Hypovitaminosis D; Diabetes-Related Anemia; Chronic Disease; Replacement; Therapy.

Introduction

Deficiency of vitamin D has become a global public health problem, with nearly 1 billion people worldwide being in a state of vitamin D insufficiency or deficiency. Vitamin D deficiency is closely related to neuropsychiatric diseases, immunocompromised autoimmune diseases, cardiovascular diseases, joint degeneration osteoarthritis, and allergic diseases. With the increasing focus on vitamin D deficiency, researchers have found that it is associated with many diseases, and after the 1980s, studies on the non-calcium effects of vitamin D have gradually been conducted [(1)].

Anemia of chronic disease (ACD) describes the impaired production of red blood cells associated with chronic inflammatory states, which includes cancer, autoimmune diseases, or chronic infection. Data show that anemia can also arise in the setting of severe acute inflammation which includes critical illness, or in case of milder but persistent inflammatory states that occur with aging, obesity, and kidney failure. Therefore, the name "anemia of inflammation" is more suitable compared to that of chronic disease [(2)].

Diabetes mellitus (DM) is a condition primarily defined by the level of hyperglycaemia giving rise to the risk of microvascular damage (retinopathy, nephropathy, and neuropathy). It is associated with reduced life expectancy, significant morbidity, and diminished quality of life [(3)].

Hematological changes in red blood cells (RBCs), white blood cells (WBCs), and the coagulation factors are shown to be directly associated with DM. Chronic hyperglycaemia, hyperosmolarity, and increased levels of advanced glycation end-products affect the RBCs. Anemia is a common hematological finding in DM patients. It is an important global public health problem, affects the lives of more than 2 billion people globally, accounting for about 30% of the world's population [(4)].

Vitamin D supplementation can ameliorate anemia by increasing the expression of erythropoietin receptors, stimulating the production of erythropoietin, reducing the secretion of pro-inflammatory mediators, and increasing sensitivity to erythropoietin [(5)].

The aim of this work was to evaluate the role of hypovitaminosis D in diabetes-related anemia of chronic disease and value of its replacement in response to therapy.

Patients and Methods

This randomized control trial study was carried out on 318 diabetic patients with both type I and II aged >18 years old, both sexes, and with diabetes- related anemia of chronic disease, conducted at after approval from the Ethical Committee Benha University Hospital (MS 5-12-2022). An informed written consent was obtained from the patient or relatives of the patients. The study was.

Study setting: This study was carried out in Internal Medicine department Benha University Hospitals.

Study period: This study was carried out from January 202٢ till January 202٣.

Exclusion criteria were other types of anemia, pregnancy, female with menorrhagia, patient with end stage renal disease, liver cell failure, and allergy to vit D.

The inclusion criteria were both type 1 and type 2 Diabetes, Age >18 years DM, Male and female.

Randomization and grouping:

Randomization was done by a computer-generated system. The list was concealed in sealed envelopes that were numbered and opened sequentially after obtaining the patient's consent. Patients were randomly allocated using computer generated randomization tables in to three equal groups; group 1 were with diabetes-related anemia of chronic disease) with normal 25 hydroxy vitamin D and received treatment for anemia, group 2 were with diabetes- related anemia of chronic disease

with low level of 25 hydroxy vitamin D, those patients was informed about using vitamin D in treatment (benefits and side effects) in addition to treatment of specific anemia ,then we assessed anemia after adequate period, and group 3 with diabetes but no anemia.

All patients were subjected to detailed history taking [Age, sex, diabetes mellitus, hypertension, cardio vascular diseases, anemia symptoms], full clinical examination: general examination including: general comment on patient conscious and mental state, vital signs: pulse, blood pressure, respiratory rate and temperature, and assessment of body mass index (BMI), and waist circumferences pallor, systemic examination: With special stress on: cardiovascular system, abdominal, chest, and neurological examination, and laboratory investigations including complete blood count (RBCs count, hematocrit & hemoglobin concentration, platelet, leukocyte, C-reactive protein, ESR, serum ferritin, serum iron, Total iron binding capacity (TIBC), 25 hydroxy vitamin D, Liver and kidney function Tests

Follow up:

We give vitamin-D supplementation to patients of group 2 for adequate period. Then, assessment the state of anemia in response to vitamin D therapy. The data was statically analyzed. We used the American Diabetes Association risk test questionnaire.

Sample Size Calculation:

Open Epi, Version 3, open-source calculator—clinical trial was used to calculate the least required sample size at 0.05 alpha error, power of 0.80 and odds ratio 0.01 (reference). The least Number is 318 patients. The three groups were randomized into 1:1:1 ratio, each 106 patients then follow up for hemoglobin concentration.

Approval code: MS 5-12-2022

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the three groups utilizing ANOVA (F) test with post hoc test (Tukey). Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test. A two tailed P value < 0.05 was considered statistically significant. Pearson correlation was used for detection of correlation between two qualitative variables in one group.

Results

In this study, 412 patients were assessed for eligibility, 58 patients did not meet the criteria and 36 patients refused to participate in the study. The remaining 318 patients were randomly allocated into three groups (106 patients in each). All allocated patients were followed-up and analyzed statistically. Figure 1

Table 1,2 showed statistically significant higher heart rate, serum ferritin CRP, ESR, HbA1C in DM group with anemia especially those with low vit D than those who did not have anemia, lower serum iron, TIBC, vit D in DM group with anemia especially those with low vit D than those who did not have anemia, however no statistically significant difference between the studied groups as regard demographic data (age, sex and type of DM), HR, RR, temperature, systolic BP, diastolic BP, BMI, WBCs, platelets, ALT, AST, urea, create.

Table 1: Demographic data, hemodynamic data, iron profile.

		Anemia and low vit D (n=106)	**Anemia and normal Vit D (n=106)**	**No anemia (n=106)**	**ANOVA P-value Post Hoc**
			Demographic data		
Age (years)		38.41±11.93	37.31±13.51	35.79±12.98	0.328
Gender	**Male**	60 (56.6%)	71 (67%)	69 (65.1%)	0.250
	Female	46 (43.4%)	35 (33%)	37 (34.9%)	
Type of DM	**T1DM**	60 (56.6%)	55 (51.9%)	53 (50%)	0.611
	T2DM	46 (43.4%)	51 (48.1%)	53 (50%)	
			Hemodynamic data		
HR (beat/min)		82.30 ± 5.76	81.39 ± 3.84	78.58 ± 5.24	**0.0001*** P1= 0.185 **P2= 0.0001*** **P3= 0.0001***
RR (cycle/min)		17.53 ±1.26	17.70 ±1.00	17.54±1.27	0.501 P1= 0.296 P2= 0.954 P3= 0.323
Temperature (°C)		37.04 ± 0.13	37.03 ± 0.12	37.03 ± 0.12	0.953 P1= 0.788 P2= 0.998 P3= 0.788
SBP (mm Hg)		126.46 ±12.19	125.23 ± 7.32	125.71±10.11	0.674 P1= 0.379 P2= 0.588 P3= 0.735
DBP (mm Hg)		82.72 ± 8.63	81.53 4.97	82.10±7.10	0.473 P1= 0.221 P2= 0.528 P3= 0.528
BMI (Kg/ m^2)		26.84 ± 3.08	27.44 3.26	26.92±4.27	0.417 P1= 0.223 P2= 0.869 P3= 0.292
Waist circumference (cm)		16.28 ± 0.92	16.37 0.88	16.38±0.41	0.553 P1= 0.363 P2= 0.331 P3= 0.950
			Iron profile		
Serum iron (mcg/dL)		25.11±8.32	28.44±5.80	41.38±10.15	**0.0001*** **P1= 0.004*** **P2= 0.0001*** **P3= 0.0001***
Serum ferritin (ng/mL)		83.80±8.39	68.62±3.35	56.51±10.23	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** **P3= 0.0001***
RBCs (*10^9/L)		311.01±45.15	338.81±37.74	343.24±23.26	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** P3= 0.379

Table 2: Blood count, renal, liver function tests, acute phase reactant, Vit D and HA1C of the studied population

	Anemia and low vit D (n=106)	Anemia and normal Vit D (n=106)	No anemia (n=106)	ANOVA P-value - Post Hoc
		Blood count		
RBCs (*10^9/L)	3.16±0.07	3.51±0.30	4.37±0.23	**0.0001*** **P1= 0.0001*** **P2=0.0001*** **P3= 0.0001***
HB (g/dl)	8.65±0.39	9.77±0.38	11.65±0.77	**0.0001*** **P1= 0.0001*** **P2=0.0001*** **P3= 0.0001***
HCT (%)	25.30±1.97	30.13±1.06	34.99±2.30	**0.0001*** **P1= 0.0001*** **P2=0.0001*** **P3= 0.0001***
WBCs (*10^9/L)	6.6953±0.75	6.8811±0.78	6.8557±0.82	0.174 P1= 0.085 P2=0.137 P3= 0.813
Platelets (*10^9/L)	329.00±59.13	336.56±68.90	325.61±75.20	0.488 P1= 0.419 P2= 0.717 P3= 0.242
		Renal and liver function tests		
ALT (U/L)	23.42 6.39	22.37 4.99	22.24 5.06	0.235 P1= 0.168 P2= 0.120 P3= 0.862
AST (U/L)	30.55±11.72	28.96±5.54	28.87±5.63	0.244 P1= 0.158 P2= 0.135 P3= 0.933
Urea (mg/dl)	27.37±9.44	28.01±9.23	25.47±4.62	0.060 P1= 0.563 P2= 0.088 P3= 0.052
Creatinine (mg/dL)	0.69±0.25	0.67±0.24	0.64±0.11	0.216 P1= 0.622 P2= 0.089 P3= 0.226
		Acute phase reactant		
CRP (mg/dL)	3.66±0.73	3.25±0.86	3.20±0.93	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** P3= 0.678
ESR (mm/hr)	17.43±4.58	16.16±4.20	15.67±3.86	0.008 P1= 0.398 P2= 0.029 **P3= 0.003***
		Vit D and HA1C		
HbA1C (%)	7.48±0.47	7.06±0.30	6.60±0.55	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** **P3= 0.0001***
Vit. D (ng/mL)	11.48±1.15	34.53±5.11	35.32±3.10	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** P3= 0.102

Data are presented as mean ± SD or frequency (%). DM: Diabetes mellites, HR: heart rate, RR: Respiratory rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, TIBC: Total iron binding capacity, RBCs: Red blood cells, HB: Hemoglobin, HCT: hematocrit, WBCs: White blood cells, ALT: Alanine transaminase, AST: Aspartate aminotransferase, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, HbA1C: Hemoglobin A1C, Vit. D: Vitamin 5-hydroxyvitamin D, *: significant P value as <0.05, P1: comparison between DM with Anemia and low vit D before treatment versus DM with Anemia and low Vit D after treatment, P2: comparison between DM with Anemia and low Vit D before treatment versus DM without Anemia, P3: comparison between DM with Anemia and low Vit D after treatment versus DM without Anemia.

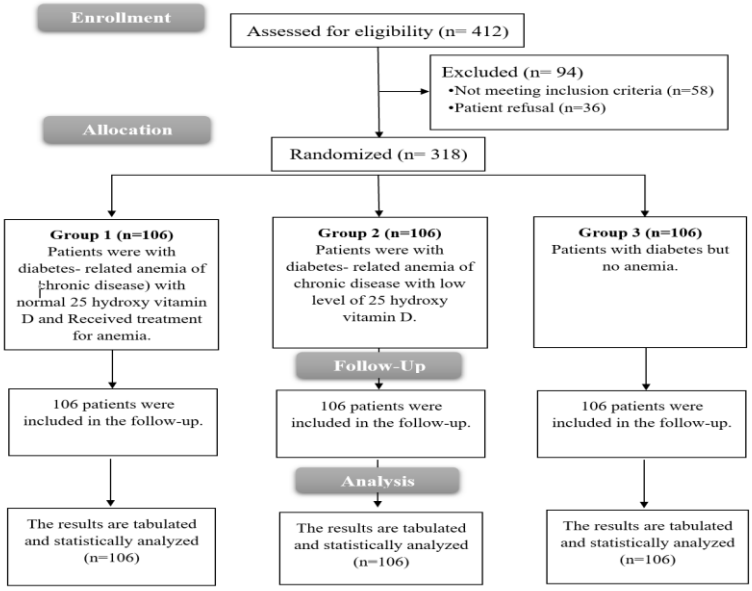

Figure 1: CONSORT flowchart of the studied patients

Table 3: The iron profile, and blood count of the studied population before and after treatment

	Anemia and low vit D before treatment (n=106)	**Anemia and low Vit D after treatment (n=106)**	**No anemia (n=106)**	**P-value Post Hoc**
		Iron profile		
Serum iron (mcg/dL)	25.11±8.32	34.11±8.32	41.38±10.15	**0.0001*** **P1= 0.0001*** **P2= 0.0001*** **P3= 0.0001***
Serum ferritin (ng/mL)	83.80±8.39	84.08±8.58	56.51±10.23	**0.0001*** P1= 0.819 **P2= 0.0001*** **P3= 0.0001***
TIBC (mcg/dL)	311.01±45.15	311.35 45.26	23.26±23.540	**0.0001*** P1= 0.950 **P2= 0.0001*** **P3= 0.0001***
		Blood count		
RBCs (*10^9/L)	3.16±0.07	3.18±0.09	4.37±0.23	**0.0001*** **P1=** 0.458 **P2= 0.0001*** **P3= 0.0001***
HB (g/dl)	8.65±0.39	8.66±0.39	11.65±0.77	**0.0001*** **P1=** 0.861 **P2= 0.0001*** **P3= 0.0001***
HCT (%)	25.30±1.97	25.35±1.90	34.99±2.30	**0.0001*** P1= 0.829 **P2= 0.0001*** **P3=** 0.216

Data are presented as mean ± SD. TIBC: Total iron binding capacity, RBCs: Red blood cells, HB: Hemoglobin, HCT: hematocrit, *: significant P value as <0.05, P1: comparison between DM with Anemia and low vit D before treatment versus DM with Anemia and low Vit D after treatment, P2: comparison between DM with Anemia and low Vit D before treatment versus DM without Anemia, P3: comparison between DM with Anemia and low Vit D after treatment versus DM without Anemia

There was a statistically significant increase in serum iron in DM group with anemia and low vit D after than those before vit D supplementation. However, serum iron after treatment still significantly lower than those without anemia. Furthermore, there was no significant difference in serum ferritin, TIBC, RBCs count, hemoglobin and HCT level before and after vit D supplementation. (Table 3)

Vitamin D serum level has statistically significant negative correlation with HBA1C, serum ferritin, heart rate, CRP, and significant positive correlation with serum iron, TIBC, RBCs, HB, and HCT. While HbA1C level has statistically significant negative correlation with serum iron, TIBC, RBCs, HB, HCT and WBCs, and significant positive correlation with serum ferritin, platelets, heart rate, CRP, ESR and waist circumference. Age, RR, temperature, SBP, DBP, BMI, ALT, AST, urea, and creatinine were insignificantly correlated. (Table 4)

Table 4: Correlation between clinical & laboratory data with serum level of vit D and HbA1C of the studied population.

	Vit. D		HA1C	
	r	**p-value**	**r**	**p-value**
HbA1C (%)	-0.508	**0.0001***	--	--
Age (years)	-0.054	0.340	-0.062	0.274
Iron (mcg/dL)	0.435	**0.0001***	-0.368	**0.0001***
Ferritin (ng/mL)	-0.715	**0.0001***	0.495	**0.0001***
TIBC (mcg/dL)	0.318	**0.0001***	-0.134	**0.017***
RBCs (*10^9/L)	0.653	**0.0001***	-0.670	**0.0001***
HB (g/dl)	0.706	**0.0001***	-0.682	**0.0001***
HCT (%)	0.769	**0.0001***	-0.704	**0.0001***
WBCs (*10^9/L)	0.099	0.077	-0.234	**0.0001***
Platelets (*10^9/L)	0.032	0.572	0.228	**0.0001***
CRP (mg/dL)	-0.205	**0.0001***	0.220	**0.0001***
ESR (mm/hr)	0.104	0.064	0.133	**0.017***
HR (beat/min)	-0.214	**0.0001***	0.225	**0.0001***
RR (cycle/min)	0.029	0.612	0.045	0.425
Temperature (°C)	-0.003	0.952	0.011	0.839
SBP (mm Hg)	-0.044	0.434	-0.010	0.853
DBP (mm Hg)	-0.051	0.362	-0.008	0.886
BMI (Kg/ m^2)	0.069	0.218	0.041	0.471
Waist circumference (cm)	0.066	0.238	0.192	**0.001***
ALT (U/L)	-0.079	0.162	0.103	0.066
AST (U/L)	-0.091	0.105	0.067	0.234
Urea (mg/dl)	-0.036	0.526	0.076	0.179
Creatinine (mg/dL)	-0.061	0.280	0.035	0.533

r: correlation coefficient, HR: heart rate, RR: Respiratory rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, TIBC: Total iron binding capacity, RBCs: Red blood cells, HB: Hemoglobin, HCT: hematocrit, WBCs: White blood cells, ALT: Alanine transaminase, AST: Aspartate aminotransferase, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, HbA1C: Hemoglobin A1C, Vit. D: Vitamin 5-hydroxyvitamin D, *: significant P value as <0.05.

Discussion

Type 2 DM is a multifactorial disease involving genetic and environmental factors. It is characterized by dysregulation of carbohydrate, lipid, and protein metabolism due to impaired insulin secretion, increased insulin resistance, or a combination of both, resulting in hyperglycemia and chronic inflammation [6].

The current study showed that there was no statistically significant difference between the studied groups as regard age,

sex and type of DM. In a study which agrees with the current study [7], it showed that there was no significant association between vitamin D level and age in patients with type 2 diabetes mellitus, but in contrast to the current study they found higher prevalence of vitamin D deficiency among females. In contrast to the current study, a previous study [8] showed that serum 25(OH)D levels were significantly correlated with age, sex and diabetes history in patients with diabetic nephropathy. The disagreement may be due to the difference in inclusion criteria.

The current study showed also that there was statistically significant higher heart rate in DM group with anemia especially those with low vit D than those who did not have anemia. However, there was no statistically significant difference between the studied groups as regards other anthropometry or vital data. The correlation analysis showed that the HR was negatively correlated with vit D level and positively correlated with HbA1C level. Chronic anemia was known to result in increased cardiac output, volume overload, increased heart rate, and ultimately progressive left ventricular hypertrophy (LVH). Anemia known to be a potent adverse risk factor for new-onset heart failure [9]. In agreement with the current study, recent research was done in 2023 [10] and showed that there was significant increase in heart rate among anemia patients with T2DM. In concordance with the current study, a previous study [11] found no significant association between blood pressure and vit D status in T2DM patients. Vitamin contrast to the current study vitamin D deficiency patients have significantly higher BMI and waist/hip ratio.

The current study showed that HbA1C level was positively correlated with waist circumference.

This comes in agreement with others [12] who revealed that there was significantly linear relationship between WC and HbA1c, which suggests that addressing central obesity issue is beneficial to people with T2DM or at risk of T2DM.

Regarding the iron profile, it was revealed that there was statistically significant lower serum iron and TIBC and higher serum ferritin in DM group with anemia especially those with low vit D than those who did not have anemia. The correlation analysis showed that the vit D level was negatively correlated with ferritin level and positively correlated with iron and TIBC. Also, the current study showed that the HA1C level was positively correlated with ferritin level and negatively correlated with iron and TIBC.

The observations of a group of researchers [13] confirmed that, there is a positive relationship between iron and Vitamin D because the haeme-bound iron is required for the hydroxylation process of Vitamin D, so variations in Vitamin D metabolism are closely linked to iron deficiency.

In concordance with the current study a group of researchers [14] showed that vitamin D was positively associated with serum ferritin levels ($p = 0.041$) among Korean women with metabolic syndrome.

The current study showed that there was statistically significant lower RBCs count, hemoglobin and hematocrit in DM group with anemia especially those with low vit D than those who did not have anemia.

The correlation analysis showed that the vit D level was positively correlated with RBCs, HB and HCT. Also, the current study showed that the HbA1c level was negatively correlated with RBCs, Hb, HCT, WBCs and Platelets. This comes in agreement with others [15] who revealed that Hemoglobin, RBC count, and erythropoietin concentrations were all positively correlated with serum 25(OH)D concentrations. These findings are suggestive of a protective role of vitamin D against drug-induced disturbances in erythropoiesis.

In addition in study done in 2022 [16] it was shown that the prediabetes patients with deficient Vitamin D level showed a significantly low mean Hb level compared

to insufficient and sufficient Vitamin D level. Also, it was shown that the Hb level was significantly impaired among T2DM patients with anemia [10].

Regarding renal and liver functions results, the current study showed that there was no statistically significant difference between the studied groups as regard renal and liver function tests. In agreement with the current study, a research done found no association between vit D level with urea or creatinine levels in T2DM patients [7]. However, according to several animal and human studies, vitamin D appears to play a significant role in the development of diabetic nephropathy. Patients with diabetes and low serum levels of vitamin D are at an increased risk of DKD and the subsequent deterioration of renal function [7, 17].

Regarding inflammatory markers, the current study showed that there was a statistically significantly higher CRP and erythrocyte sedimentation rate (ESR) in DM group with anemia especially those with low vit D than those who did not have anemia.

The correlation analysis showed that the vit D level was negatively correlated with CRP level and positively correlated with ESR level. Also, the current study showed that the HA1C level was positively correlated with CRP and ESR levels. In concordance with the current study 0. concluded that ESR is higher in T2DM patients with vitamin D deficiency than patients with sufficient vitamin D. There was an inverse association between ESR and vitamin D levels [18].

The present study showed that there was statistically significantly lower vit D and higher glycosylated hemoglobin (HbA1c) in DM group with anemia especially those with low vit D than those who did not have anemia. The correlation analysis showed that the vit D level was negatively correlated with HA1C. In agreement with the present study it was shown that a negative correlation existed between 25 (OH) D and HbA1c in T2DM subjects. [7] Similarly, other scientists showed that there was also an inverse linear relationship between vitamin D with HbA1C and FBS [19].

Serum 25(OH)D levels were significantly correlated with HbA1c (8). Moreover, HbA1c was independent risk factors of 25(OH)D deficiency in diabetic nephropathy. In contrast to others [10] who found no significant association between anemia and HbA1c level in patients with type 2 diabetes mellitus.

Deficiency of vitamin D is common in diabetics which may lead to uncontrolled diabetes. However, vitamin D supplementation in diabetics can be helpful in achieving adequate glycemic level. Here the current study showed that there was statistically significant increased serum iron in DM group with anemia and low vit D after than those before vit D supplementation. However, serum iron after treatment is still significantly lower than those without anemia. Furthermore, there was no significant difference in serum ferritin and TIBC before and after vit D supplementation. Also, the current study showed that there was no significant difference in RBCs count, hemoglobin and HCT level before and after vit D supplementation.

To the best of our knowledge this is the first trial assessing the effect of vit D supplementation on serum iron, serum iron, HCT level in diabetic patients with anemia.

A systematic review and meta-analysis showed that vitamin D supplementation leads to a non-significant reduction in hemoglobin levels in subjects (17.5–68 years old) [P = 0.95], also it has no significant effect on ferritin concentrations [P = 0.91]. However, vitamin D supplementation demonstrated positive effects on transferrin saturation [P = 0.01] and iron status [P = 0.002], which support our findings [20].

Limitation: The current study was limited by small sample size, being a single center study and relatively short follow up period,

and further comparative studies with larger sample size and longer follow-up are needed to confirm our results and to identify risk factors of vit D deficiency.

We recommended that further studies with larger sample size are needed to confirm the current results, with longer follow-up are needed to evaluate the role of hypovitaminosis D in diabetes- related anemia of chronic disease and value of its replacement in response to therapy, it is recommended that future studies be conducted using well-designed randomized controlled trials or large, comparative observational studies, inclusion a representative sample of patients with similar age, gender, and disease severity, the sample size of future studies should be large enough to provide meaningful conclusions and to control for confounding factors, to accurately assess long-term outcomes, studies should have a longer follow-up period, and research should include multicenter studies to validate our findings.

Conclusion

The current study suggested that there was a close relationship between vitamin D deficiency and anemia in diabetic patients.

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