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Therapeutic Fasting and Vitamin D Levels: A New Dimension in Type 2 Diabetes Mellitus Prevention and Management—A Brief Report

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Abstract

Introduction Studies link hypovitaminosis D to be significantly associated with poor glycemic control, heightened inflammation, and risk of complications. Studies recommend fasting or calorie restriction as a useful measure to achieve diabetic reversal. The present study explores if therapeutic fasting is associated with improvement in the vitamin D levels and other clinical outcomes related to type 2 diabetes mellitus (T2DM).

Methods This observational study included 26 T2DM patients exposed to a 10-day medically supervised fasting (≈ 500–1000 Kcal/day) in a complementary medicine facility. Levels of vitamin D, B12, fasting blood sugar (FBS), blood pressure, anthropometric measures, World Health Organization Quality of Life, disease perception (Brief Illness Perception Questionnaire), and self-reported vitality were measured at the baseline and the 10th day.

Results Significant improvement in the levels of vitamin D ($p = 0.000$), B12 ($p = 0.03$), and reduction in FBS levels ($p = 0.001$), blood pressure, body mass index, waist and hip circumference ($p \leq 0.05$), and improvement in quality of life, vitality, and disease perception ($p < 0.001$) were observed by the end of 10th day. FBS shared a negative correlation with vitamin D levels (males $r = -0.1$, females $r = -0.48$).

Conclusion The present findings provide insights into the probable mechanisms by which therapeutic fasting modulates the progression of T2DM. Nevertheless, large-scale randomized controlled trials are warranted to validate the present findings.

Keywords
- vitamin D deficiency
- type 2 diabetes mellitus
- vitamin B12
- insulin resistance
- fasting
- calorie restriction

Introduction

India is considered the "diabetic capital of the world," with more than 74 million type 2 diabetes mellitus (T2DM) patients living in the country.[1] Recent evidence suggests a higher prevalence of hypovitaminosis D among T2DM patients, which is associated with insulin resistance.[2,3] Polymorphisms in vitamin D receptor genes have been linked to impaired insulin secretion and function. This is mainly because of vitamin D's action on calbindin, the calcium binding protein which controls the function of insulin by regulating calcium ions.[4,5] Vitamin D further protects the β-cells in the pancreas from β-cell cytokine-induced apoptosis by altering the expression of cytokines. This has an important role to play in the progression of T2DM, as systemic inflammation promotes insulin resistance and can lead to the worsening of T2DM.[6,7]

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Therefore, maintaining optimal levels of vitamin D may help in preventing the incidence and progression of T2DM and its associated complications. In the prediabetic population, vitamin D supplementation has been shown to reduce the risk of diabetes mellitus by 10 to 13% when compared with a placebo.[8] Therapeutic fasting has increasingly become popular among health care providers and patients as a lifestyle regimen that has multidimensional benefits.[9] Recent evidence suggests therapeutic fasting is a safe and beneficial modality among T2DM patients.[10] Insulin resistance which is linked to diabetes is characterized by heightened inflammation in the body, elevated C-reactive protein, and decreased adiponectin.[6] One of the many advantages of calorie restriction is the stimulation of the activated protein kinase (AMPK) pathway, which helps with glucose regulation and increases insulin sensitivity. Fasting has been attributed to bringing positive changes in adiponectin and leptin, all of which are linked to bringing favorable changes in diabetes-related outcomes.[7] Intermittent fasting has been shown to promote weight loss, enhance cellular autophagy, decrease inflammatory cytokines, and lower advanced glycated end products.[8] Therapeutic fasting has been shown to increase vitamin D levels in both healthy volunteers and chronic disease patients.[11–13] However, the role of therapeutic fasting in improving the vitamin D levels in T2DM patients is less understood. The present observational study is therefore intended to explore if the 10-day medically supervised fasting (MSF) has any potential impact on vitamin D, vitamin B12, fasting blood sugar levels, anthropometric measures, quality of life, and disease perception in T2DM patients.

Materials and Methods

This prospective longitudinal observational study was conducted at a residential complementary and alternative medicine setting in North India and was approved by the institutional ethics committee of the study setting. We followed up on 26 participants, both males and females, diagnosed with T2DM who participated in a 10-day MSF program. These participants were selected from a larger cohort of 106 patients with diverse medical conditions who enrolled in a voluntary fasting regimen organized at a complementary and alternative medicine setting. We excluded individuals with type 1 diabetes mellitus, any other metabolic disorders other than T2DM, any known nutritional deficiency, those who were on insulin, and those already taking vitamin D and vitamin B12 supplements.

All 26 participants signed an informed consent and underwent a 10-day period of MSF, which consisted of three phases: the preparation phase (days 1, 2, and 3), the fasting phase (days 4 through 7), and the refeeding phase (days 8, 9, and 10). Calorie consumption was gradually reduced until day 3, followed by a 4-day fast on juice, soups, and lemon honey water. Calories were gradually increased in the same manner from day 8 to 10 (see ►**Fig. 1**). The fasting regimen was designed by the treating physicians in the study setting, and the investigators were not involved in the design or delivery of the fasting program. The participants continued their oral antidiabetic medications and few of the patients' medication doses were tapered by their treating physicians after monitoring their blood sugar levels.

Blood samples were collected for measuring the biochemical variables such as fasting blood sugar (photometry technique: GOD-PAP method), serum total 25-hydroxy vitamin D level (fully automated chemiluminescent immune assay method), and vitamin B12 (competitive chemiluminescent immune assay method). Apart from this we recorded blood pressure and anthropometric measures like body mass index (BMI) and waist and hip circumference from all the participants.

Additionally, the impact of MSF on the participants' self-perceived vitality (energy levels) was measured using a visual analog scale (VAS), quality of life using World Health Organization Quality of Life questionnaire, and disease perception using a Brief Illness Perception Questionnaire. All these measures were collected at two time points, day 1 (before the fasting) and day 10 (after the fasting). Further, we also collected the details regarding any events of hypoglycemia to measure the safety of the participants undergoing MSF by using a daily diary.

Statistical Analysis

The data was cleaned and analyzed using Statistical Package for Social Sciences (SPSS) version 27. The sample characteristics were analyzed descriptively employing grouped frequencies and percentages. Since the key study variables (such as fasting blood sugar, BMI, vitamin D, etc.) were captured as continuous variables, the means and standard deviation at baseline and postintervention were computed and compared. The normality of the variables was assessed using Shapiro–Wilk test. The variables which were found to be normally distributed at baseline and postintervention were analyzed using a paired *t*-test. The variables which were not normally distributed (i.e., $p < 0.05$ as per Shapiro–Wilk test) were analyzed using related samples Wilcoxon signed ranked test.

The effect size was computed employing Cohen's d using sample standard deviation of the mean difference adjusted by the correlation between measures. Additionally, comparisons were made between the case-wise variations in fasting blood sugar and vitamin D levels using radar charts. Pearson's correlation coefficient was computed between the postintervention fasting blood sugar and vitamin D levels separately among males and females. The significance level (α) was set at 0.05.

Results

There were 14 females (53.8%) and 12 males (46.2%), who were mostly from the middle class (92.3%) and upper class (7.7%). The majority of study participants (61.5%) were over the age of 51, with the remainder (38.5%) being under the age of 50. Around 97% of participants reported that they do not use tobacco or alcohol. All the participants were on antidiabetic medications. During the 10-day fast, none of the participants reported any hypoglycemia episodes.

A significant difference was observed in fasting blood sugar levels ($p = 0.001$), serum vitamin D ($p < 0.001$), and other study parameters assessed (see ►**Table 1**). Among the participants

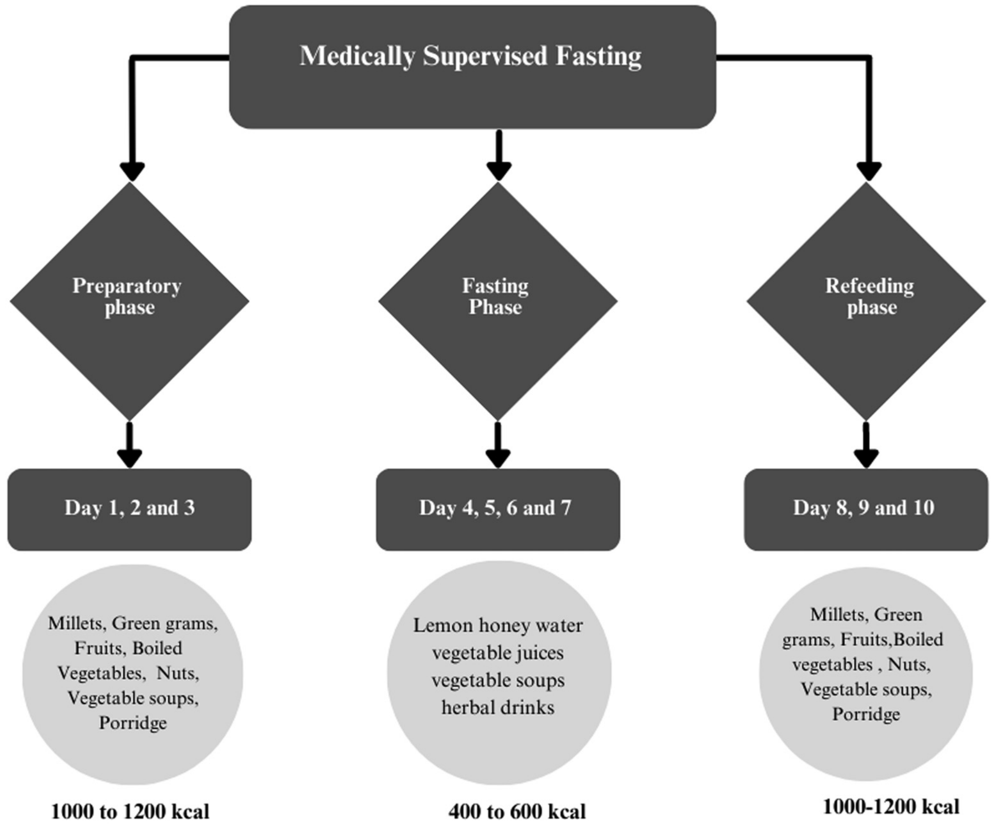

Fig. 1 Overview of medically supervised fasting regimen.

studied, the fasting blood sugar levels showed a significant decrease whereas the vitamin D levels showed a significant increase. It was also found that there was a negative correlation ($r = -0.48$) between postintervention vitamin D and blood sugar levels among female participants (see ►**Fig. 2**).

Discussion

The present study demonstrates that a 10-day medically supervised fast can improve the vitamin D levels of T2DM patients and reduce fasting blood sugar levels, in addition to other favorable clinical and mental health outcomes. A recent review suggests therapeutic fasting is a safe and useful regimen in T2DM that not only improves glycemic control but also reduces the need for antidiabetic medication.[10] Another systematic review and meta-analysis on fasting and T2DM found that fasting lowers BMI, insulin resistance, glycated hemoglobin levels (HbA1C), blood glucose levels, leptin, and increases adipokine concentration.[14,15] These evidences indicate a positive role of therapeutic fasting in T2DM.

Our observation suggests a 10-day supervised medical fasting can improve vitamin D levels. We also found a negative correlation between vitamin D levels and fasting blood sugar levels. Earlier studies also reported MSF up to 10 days can improve the vitamin D levels.[11–13] A growing body of literature suggests the role of vitamin D in improving type 2 diabetes-related clinical outcomes by attenuating insulin resistance and priming the endocrine functions of the pancreas.[2,4,5] A meta-analysis study revealed the beneficial effect of vitamin D in reducing fasting blood sugar, glycated hemoglobin levels (HbA1C), and insulin resistance (HOMA-IR) in patients with diabetes mellitus and deficient vitamin D status.[22] Further, vitamin D is also proven to be protective against diabetes-related complications such as neuropathy, retinopathy, and nephropathy.[21] The prevalence of hypovitaminosis D among T2DM and its impact on the progression of the disease are well documented.[3,16] T2DM patients with hypovitaminosis D are shown to exhibit higher levels of HbA1C and inflammation that worsen the prognosis of T2DM.[17,18] Fasting improves vitamin D levels by acting on adipose tissue, where the majority of vitamin D is stored.[19] Further, prolonged fasting is known to regulate the circulating inflammatory cytokines.[20] Given the inverse relationship vitamin D shares with inflammation,[21] a reduction in inflammation following fasting may be another possible mechanism by which fasting upregulates vitamin D levels.[20,21] Therefore, maintaining optimal levels of vitamin D may help in preventing the incidence and progression of T2DM and its associated complications.

Table 1 Summary of changes before and after fasting in the biochemical, anthropometric, and quality of life markers ($n = 26$)

Dependent variable	Preintervention	Postintervention	Cohen's *d*[a]	*p*-Value[b]
FBS levels	156.59 (±48.03)	133.50 (±24.08)	0.45	0.001
Body mass index	30.09 (±5.71)	28.80 (±5.15)	0.21	0.000
Waist circumference	39.56 (±4.06)	38.11 (±4.30)	0.33	0.000
Hip circumference	41.84 (±4.84)	41.00 (±4.88)	0.17	0.005
Systolic BP	127.69 (±14.40)	123.00 (±8.38)	0.37	0.051
Diastolic BP	81.92 (±8.44)	77.92 (±6.71)	0.36	0.012
Vitamin D	18.19 (±10.52)	22.29 (±11.81)	−0.35	0.000[c]
Vitamin B12	348.00 (±337.24)	394.88 (±271.34)	−0.15	0.030[c]
Hemoglobin	12.97 (±2.08)	12.62 (±2.48)	0.15	0.266
Physical QoL	64.69 (±18.81)	77.35 (±14.64)	−0.72	0.000
Psychological QoL	63.58 (±16.25)	79.69 (±13.9)	−1.05	0.000
Social QoL	72.73 (±13.65)	82.58 (±12.64)	−0.73	0.000
Environmental QoL	75.19 (±15.22)	81.62 (±13.7)	−0.44	0.001
Vitality VAS	6.23 (±1.42)	8.23 (±0.82)	−1.62	0.000
Disease perception	52 (±8.17)	46.35 (±8.75)	−0.67	0.000

Abbreviations: BP, blood pressure; FBS, fasting blood sugar; QoL, quality of life; VAS, visual analog scale.
[a]Cohen's *d* was calculated as the measure of effect size using sample standard deviation of the mean difference adjusted by the correlation between measures.
[b]Paired *t*-test was used to assess the difference between the means of dependent variables in the above table.
[c]*p*-Value computed based on related samples Wilcoxon signed ranked test.

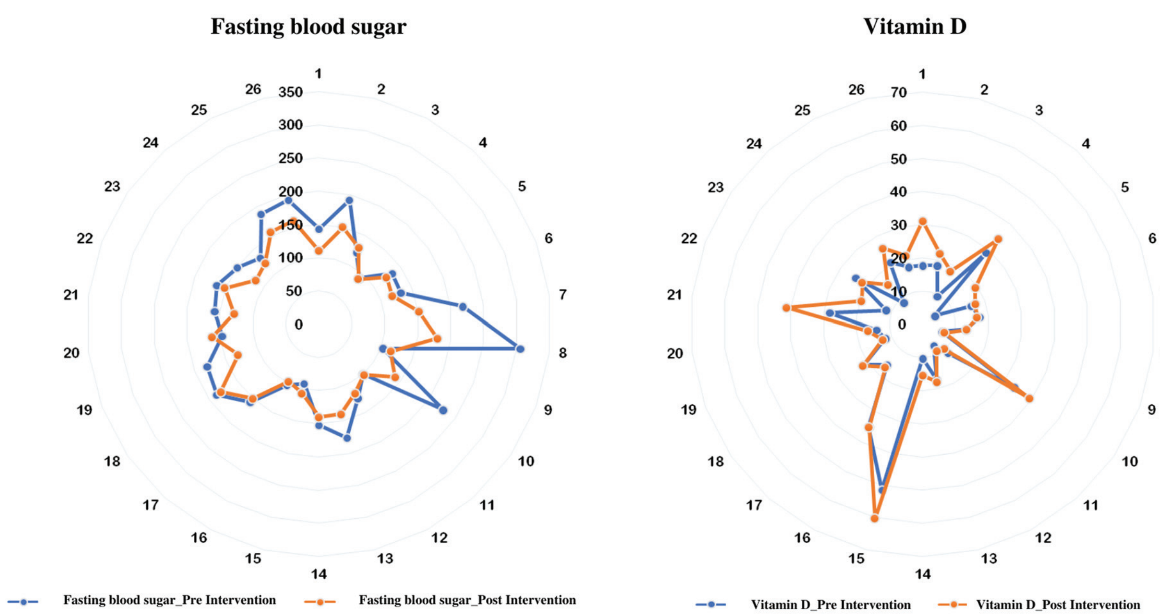

Fig. 2 Changes in fasting blood sugar and vitamin D among the study participants.

We also observed a significant improvement in the vitamin B12 levels of our study participants. Like vitamin D, deficiency of vitamin B12 is also commonly prevalent among the T2DM patients.[22] The deficiency of vitamin B12 among T2DM patients is commonly linked to the use of metformin[23] which increases with the age of the patient, the duration of metformin use, and its dose.[24] Vitamin B12 deficiency can lead to macrocytic anemia, cognitive deficits, and neuropathy[24] which are commonly seen in T2DM patients and therefore need immediate attention.

Studies suggest that an adequate intake of calcium can reverse the vitamin B12 malabsorption and subsequent deficiency induced by metformin.[25] Similarly, adequate vitamin D can enhance calcium absorption from the intestine by promoting active calcium transport and improving calbindin's synthesis.[26] Our study participants have shown an increasing trend in both vitamin D and vitamin B12 levels. The impact of vitamin D on calcium levels and its further role on vitamin B12 absorption may be the reason for the upregulation of vitamin B12 in our study participants. This demonstrates that therapeutic fasting can play a broader role in T2DM patients in negating the side effects of antidiabetic medications in addition to the clinical-related outcomes.

We observed significant reductions in the blood pressure, BMI, and waist and hip circumference among the study participants. Elevated blood pressure, body weight, and waist and hip circumferences are attributed to poor glycemic control and lead to the incidence of diabetic complications and cardiovascular disease.[27] Our findings also support previous findings that fasting can reduce anthropometric measurements and prevent cardiovascular complications.[10,27]

No adverse events or hypoglycemic events were reported by the study participants during the entire duration of the fasting program. This may be due to the monitoring support provided by the lifestyle physicians who were involved in the fasting delivery. An earlier study on fasting in diabetes patients suggested that supervision during fasting may help reduce adverse hypoglycemic events.[28]

T2DM is associated with severe impairment in the quality of life of the patients that affects their social, economic, and general well-being. A recent review suggested the need for research and interventions that can improve the quality of life among T2DM patients.[29] Therapeutic fasting is known to improve the quality of life and general well-being.[30] Our inferences indicate that fasting is associated with significant improvements in perceived energy levels, quality of life, and disease perception. This suggests fasting as a potential holistic tool that can be integrated into the management of diabetes.

Study Limitations

Even though the observations favor the introduction of MSF as an adjuvant therapy in T2DM, there are demonstrable limitations in this study. Lack of a control group, limited sample size, and lack of follow-up may significantly limit the generalizability and decisiveness of the present inferences. Our limited sample size is mainly due to the conduct of study in a single clinical setting and exclusion criteria adopted. Future studies are needed employing a larger sample size. Furthermore, we did not collect any data regarding sunlight exposure, exercise, and types of oral hypoglycemic medications and dosage during the study period which may be considered as a potential confounder. It would have been also beneficial to collect other vital metabolic parameters like postprandial blood sugar, lipid profile, corrected calcium, etc. for identifying more intriguing conclusions. Therefore, the current findings need to be validated with robust clinical trials in other settings with longer follow-up periods. Nonetheless, the current findings provide intriguing insights into the utility of including therapeutic fasting in the prevention and management of T2DM (see ►**Fig. 3**).

Conclusion

Therapeutic fasting is known to have potential benefits for those with metabolic disorders. Evidence suggests that fasting could contribute to reducing the symptoms and clinical progression of T2DM. The findings of this study shed light on

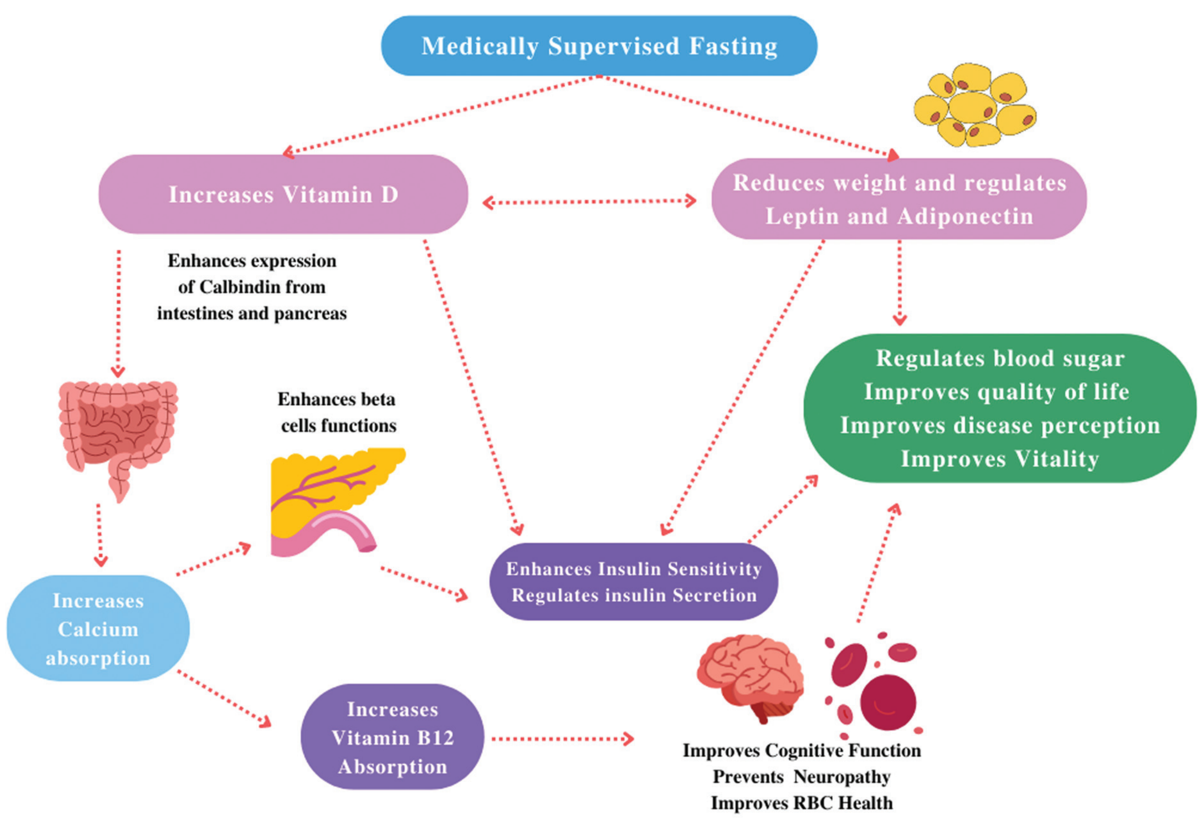

Fig. 3 Probable mechanism behind fasting and improvement in diabetes-related outcomes.

possible mechanisms by which therapeutic fasting may influence the course of T2DM, one of which could be an increase in vitamin D and B12 levels. However, the limitations of the present study warrant large-scale randomized controlled studies to verify the current findings.

Ethics Approval

The study was approved by the institutional ethics committee of Sant Hirdaram Medical College for Naturopathy & Yogic Sciences (F.No:12/SHMCNYS/IEC/P35), Bhopal, Madhya Pradesh, India.

Consent to Participate

All the participants signed a written consent to express their consent to participate in the study.

Availability of Data and Material

The data will be made available on request to the corresponding author.

Conflict of Interest

The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

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