CME/CE/MOC Offering

Gunadhar Panigrahi, MD,
Sally M. Goodwin, CCMA,
Kara Livingston Staffier, MPH,
and Micaela Karlsen, PhD

Remission of Type 2 Diabetes After Treatment With a High-Fiber, Low-Fat, Plant-Predominant Diet Intervention: A Case Series

Abstract: **Background:** *Prevalence of type 2 diabetes (T2D) is rising, and its burden on the healthcare system remains a challenge. Consumption of a plant-predominant diet is a promising approach for achieving remission, which has emerged as a therapeutic target.* **Objective:** *To establish feasibility of achieving T2D remission with a plant-predominant diet in a cohort of free-living individuals.* **Methods:** *Patients referred to a wellness clinic were treated with a low-fat, whole food, plant-predominant diet while receiving standard medical treatment. Included patients were adults, mostly elderly, with HbA1c > 6.5%, with or without use of antidiabetic medications.* ***Results:*** *N = 59 patients were included in this analysis, with mean age 71.5 years (range 41-89). Twenty-two (37%) patients achieved T2D remission. Mean differences showed a significant decrease post-lifestyle change (T2) compared to prior to lifestyle change (T1) for the following outcomes [least squares mean difference (95% CI)]: BMI [−2.6 (−4.8, −.3)] kg/m^2; HbA1c [−1.3 (−1.6, −1.0)] %; and fasting glucose [−29.6 (−41.8, −17.5)] mg/dL. No significant differences were observed for systolic or diastolic blood pressure, HDL, LDL, or triglycerides.* ***Conclusion:*** *A lifestyle-based treatment intervention promoting adherence to a plant-predominant diet and integrated as part of routine care can successfully achieve T2D remission in wellness clinic patients.*

Keywords: type 2 diabetes; remission; plant-based diet; body mass index; hemoglobin A1c; antidiabetic medications

> "A significant reduction in body weight, especially greater than 15 kg compared to baseline, was highly predictive of remission of T2D."

Introduction

Diabetes is the most prevalent non-communicable disease in the world. In the US, from 2001 to 2020, the incidence of diabetes significantly increased in adults 18 or older. A total of 37.3 million people have

DOI: 10.1177/15598276231181574. Sentara Cardiology Specialists Wellness Clinic, Sentara Princess Anne Hospital, Virginia Beach, VA, USA; Sentara Cardiology Specialists Wellness Clinic, Sentara Princess Anne Hospital, Virginia Beach, VA, USA; and American College of Lifestyle Medicine, Chesterfield, MO, USA. Address correspondence to: Micaela Karlsen, PhD, American College of Lifestyle Medicine, PO Box 6432, Chesterfield, MO 63006, USA. e-mail: mkarlsen@lifestylemedicine.org.

diabetes, which is 11.3% of US population.[1] Moreover, if untreated, prediabetes gradually progresses to overt type 2 diabetes (T2D) over time, which comes with a range of complications including cardiovascular disease, retinopathy, nephropathy, neuropathy, peripheral vascular disease, ischemic gangrene, limb amputation, stroke, and substantial morbidity and mortality.[2,3] The epidemic of T2D and its complications pose a major threat to global health as well as a significant economic burden to society with the economic burden worldwide being estimated to rise to over $2 trillion by 2030.[2,4,5]

The International Diabetes Federation estimated that 1 in 11 adults aged 20-79 years (415 million adults) had diabetes mellitus globally in 2015. Over 90% of diabetes mellitus cases are T2D.[2] Lifestyle changes are known to have a profound and positive effect in prevention of T2D.[6] Nutrition therapy may improve glycemic control and diabetes outcomes.[7] Plant-predominant diets, particularly healthy plant-predominant diets composed of foods such as fruits, vegetables, legumes, and whole grains, are protective against T2D.[8] However, the frequent consumption of refined and low-quality carbohydrates, processed foods, sodium, and meat increases the risk of developing diabetes.[9,10]

Despite many advances in the pharmacologic management of T2D, prevalence has continued to rise,[11] with T2D often leading to intensification of pharmacological treatment over time.[12] Consequently, there is an urgent need for simple and accessible approaches to reverse this trend, including therapeutic lifestyle change. Our previous work has identified an appropriately planned, nutrient-dense, low-fat, high fiber, plant-predominant diet to be promising in preventing and reversing T2D.[13]

The objective of this case series is to demonstrate the feasibility of medication reduction and remission using lifestyle-based intervention without drastic energy restriction among a subset of patients with T2D at a medical clinic in the Eastern US. This case series represents an example set of patients for whom clinically meaningful improvements in BMI, HbA1c,: and fasting glucose were observed after treatment with a lifestyle intervention focusing on a low-fat, whole food, plant-predominant diet, even among some with advanced age.

Methods

In the cardiovascular wellness clinic, patients are treated for heart disease, hypertension, hyperlipidemia, obesity, and diabetes and are presented with a lifestyle treatment intervention as described in greater detail below. During and after the intervention, medications are deescalated or discontinued, if needed, as blood glucose levels improve. This case series describes a purposive sample of patients who were treated at the clinic between 2007 and 2021. Electronic health records (EHR) were reviewed by the physician (G.P.) to identify eligible patients, defined as those who made lifestyle changes to adopt the recommended plant-predominant diet and had achieved meaningful improvements in HbA1c or blood glucose control and, in some cases, remission of T2D. Eighty patients who made such improvements during the 14-year time period were identified for potential inclusion. Data were extracted from the EHR via entry in Microsoft Excel and included the following: body mass index (BMI), systolic and diastolic blood pressure (SBP, DBP), HemoglobinA1c (HbA1c), fasting blood glucose (FBG), LDL cholesterol, HDL cholesterol, triglycerides, and prescriptions for insulin and oral diabetes. Data were extracted for two timepoints, the period immediately prior to lifestyle treatment (T1) and most recent follow-up post-intervention (T2). Data at T1 may have been collected at the time of visit to the wellness center or transferred from a previous practice. After further exclusion of patients with missing HbA1c at T1 or T2 (n = 16), HbA1c < 6.5 and no reported diabetes medication use at T1 (n = 1), and patients with less than 6 months between T1 and T2 (n = 4), 59 patients remained in the sample. Patients were defined as achieving remission using the consensus definition published by the American College of Lifestyle Medicine in 2021: HbA1c < 6.5% for at least 3 months with no surgery, devices, or active pharmacologic therapy for the specific purpose of lowering blood glucose.[14] Accordingly, patients meeting the criteria of HbA1c < 6.5% with no reported medications at T2 were identified, and EHR data was accessed for those patients to determine whether HbA1c < 6.5% was achieved at a timepoint at least 3 months prior to T2 with no medications. Patients were asked for permission for their deidentified data to be included in this analysis and provided either written or verbal consent. This study was approved by the University of New England IRB.

In the wellness clinic, patients are educated on the merits of adopting a plant-predominant diet, addressing major risk factors, and avoiding the complications associated with cardiovascular disease and diabetes by using the American Heart Association (AHA) Simple 7 guidelines.[15] Patients did not self-select into a designated lifestyle medicine treatment program but were simply presented with lifestyle prescriptions as part of their routine

Table 1.

Health Outcomes Pre-Dietary Intervention (T1) and Post-Dietary intervention (T2).

	N	Immediately prior to lifestyle change (T1)	≥6 months post-lifestyle change (T2)	Mean within subject change (95% CI)[a]	*P*-value
		Mean (SD)	Mean (SD)		
BMI (kg/m^2)	58	32.7 (6.4)	30.1 (6.0)	−2.6 (−4.8, −.3)	**.025**
Hemoglobin A1c (%)	59	7.3 (1.0)	6.0 (.5)	−1.3 (−1.6, −1.0)	**<.0001**
Fasting glucose (mg/dL)	54	138.0 (40.7)	108.3 (18.8)	−29.6 (−41.8, −17.5)	**<.0001**
Systolic BP (mmHg)	58	129.6 (16.9)	133.1 (17.0)	3.4 (−2.8, 9.7)	.281
Diastolic BP (mmHg)	58	73.1 (9.9)	72.8 (9.4)	−.3 (−3.6, 2.9)	.851
HDL cholesterol (mg/dL)	58	43.4 (10.1)	45.3 (11.6)	1.8 (−1.5, 5.2)	.279
LDL cholesterol (mg/dL)	58	81.8 (33.1)	72.5 (24.6)	−9.2 (−19.9, 1.5)	.090
Triglycerides (mg/dL)	58	211.1 (410.9)	112.4 (53.5)	−98.7 (−207.1, 9.7)	.074

[a]age and sex-adjusted differences of least squares means.

care. They are instructed to: (1) avoid all tobacco products, (2) maintain ideal BMI (body mass index in kg/m^2) of less than 25, (3) engage in regular exercise of minimum 150 minutes per week, and (4) follow a low fat, whole food, plant-predominant diet, (5) achieve total cholesterol of less than 200 mg/dl, triglycerides less than 150 mg/dl, HDL cholesterol greater than 40 mg/dl for men and 50 mg/dl for women, LDL cholesterol less than 100 mg/dl, without medications, (6) achieve a blood pressure of 120/80 mm of Hg or less, without medications, and (7) achieve fasting blood glucose of less than 100 mg/dl (HbA1c < 6.0%) without medications.

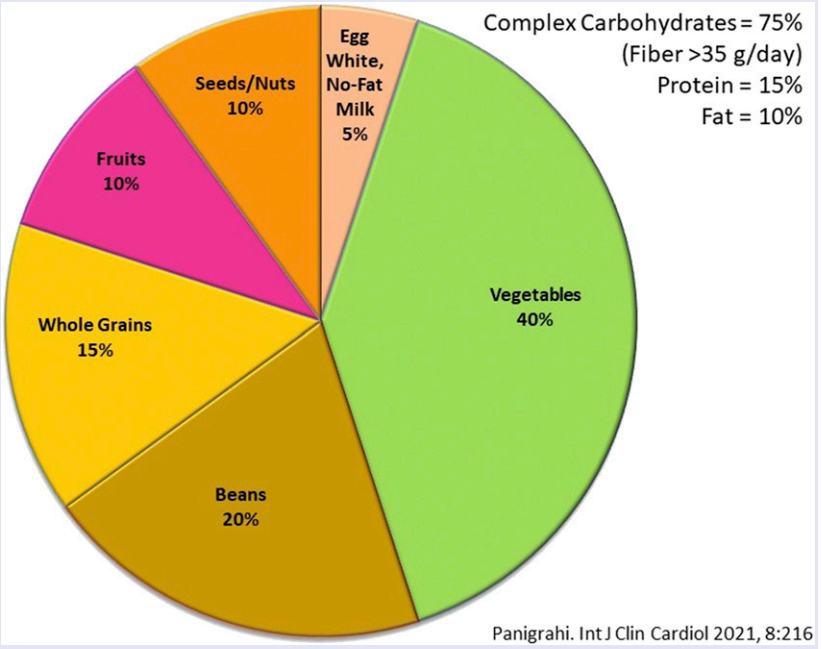
The initial patient encounter is a one-hour consultation with a physician (G.P.). This includes taking a detailed medical history with emphasis on personal and family history of diabetes and an appraisal of dietary and physical activity habits. In addition, associated comorbidities, including coronary artery disease, blood pressure control, lipid status, elevated fasting blood glucose levels, and HbA1c are appraised.

The consultation includes education on the relationship of overweight and obesity leading to type 2 diabetes. This includes the pictorial demonstration and explanations on accumulation of ectopic fat as the proximate cause of T2D and, secondly, how a sedentary lifestyle adversely contributes to this condition. Using drawings and pictures, patients are educated about how weight loss with a plant-predominant diet, along with physical activity, can reverse diabetes.[16,17] Since excess weight is a major problem with most of the patients, they are asked to set a weight loss goal to achieve success in remission of diabetes (usually 10% of body weight).

The prescribed plant-predominant diet, is low-fat and high in fiber, consisting of vegetables, legumes, whole grains, fruits, nuts, and seeds, similar to the Pritikin[18] diet. On the prescribed plant-predominant diet, 75% of calories are derived from complex carbohydrates, 15% from protein (plant), and 10% from fat (Figure 1). Patients are instructed to avoid animal-derived products, processed foods, and added fats/oils. A small quantity of egg white and no-fat dairy is allowed (approximately 5% of total calories) for occasional use. A maximum of one glass of red wine for women and two glasses for men are allowed for most days of the week. However, if weight loss is the primary goal, use of alcohol is discouraged. Patients are provided with teaching materials

Figure 1.

Dietary and nutrient composition of intervention diet.



in the form of leaflets, brochures, meal plans, and other resources to improve their learning and adoption of this diet.

Blood outcomes, including fasting blood glucose, fasting lipid profile, and HbA1c, are collected at the initial visit along with follow-up visits through nationally accredited laboratories (Sentara laboratories and LabCorp laboratories). In selected cases, C-peptide level, total and free insulin levels, and CRP are measured. A second patient encounter typically occurs approximately 6-12 weeks after the initial encounter, during which time progress is discussed and additional education is provided as needed in areas where patient has not made satisfactory progress, as defined by the AHA's 7 metrics as outlined above. Educational handouts are provided in an education materials folder. Thereafter, clinic visits are arranged every 3-6 months based on individual need. In addition, patients are encouraged to contact the clinic either by phone or by "My Chart" messaging system for any questions, concerns or guidance with respect to maintaining the prescribed diet.

Data analysis for this case series was performed in SAS (Version 9.4). A mixed linear model was performed to assess differences of least squares means, adjusted for age and sex, at T1 vs T2. As this is a case series, a complete case analysis is presented; however, an intent-to-treat analysis was done post-hoc and produced similar estimates and statistical significance (data not shown). McNemar's test was used to compare the number of patients on both insulin and oral medications at T1 and T2. A *P*-value of less than .05 was considered statistically significant.

Results

This analysis includes n = 59 patients engaged in the wellness clinic for greater than or equal to 6 months during the period of 2007-2021 and identified as showing positive improvements in diabetes status following lifestyle treatment. Mean (SD) age of included patients was 71.5 (9.7) years, ranging from 41 to 89 years, and n = 35 (59%) of patients were male. Mean time between T1 and T2 was 4.2 years (range 6 months-14 years). Based on data extracted from the EHR, 34 (58%) had a previous diagnosis of coronary artery disease, 18 (31%) congestive heart failure, 9 (15%) atrial fibrillation, 58 (98%) hypertension, 59 (100%) high cholesterol, 8 (14%) peripheral arterial disease, 4 (7%) cerebrovascular accident, and 18 (31%) chronic kidney disease. With respect to additional diabetes-related complications, 6 (10%) had been diagnosed with retinopathy, 8 (14%) with neuropathy, 2 (3%) had a history of both osteomyelitis and amputation.

When adjusted for age and sex, the mean difference showed a significant decrease for three outcomes [least square mean difference (95% CI): BMI [−2.6 (−4.8, −.3)] kg/m^2; HbA1c [−1.3 (−1.6, −1.0)] %; and fasting glucose [−29.6 (−41.8, −17.5)] mg/dL from T1 to T2. No significant differences were observed for systolic or diastolic blood pressure, HDL, LDL, or triglycerides (Table 1).

A total of n = 40 patients were prescribed glucose-lowering medications (insulin or oral agents) immediately prior to lifestyle change. This number decreased to n = 29 post-lifestyle change (*P* = .008). The number of insulin prescriptions decreased from n = 4 prior to lifestyle change to n = 1 post-lifestyle change. At T2, a total of n = 27 (46%) patients had discontinued all medications

with HbA1c < 6.5%. Twenty-two of these patients met the definition of remission upon assessment of an intermediate timepoint prior to T2 to determine whether HbA1c was less than 6.5% for at least 3 months, signifying overall remission of 37%. Mean time since achieving remission was 1.7 years (range 3 months-3.3 years). Pre-intervention, n = 7 of this group had been taking medications (oral agents), and HbA1 ranged from 5.4 to 10.1% (mean ± SD = 6.9 ± .9). Post-intervention, mean HbA1c ranged from 4.8% to 6.3% without medications (mean ± SD = 5.9 ± .4).

Discussion

This case series demonstrates that prescribing a high-fiber, low-fat, whole food, plant-predominant diet can facilitate lifestyle change and achieve remission of T2D in free-living individuals. Previous work has indicated that plant-predominant diets can improve diabetes outcomes; however, these studies have largely involved calorie restriction and/or fasting or have not identified remission as a primary outcome.[19-22] The DIRECT study found that a very low-energy diet achieved T2D remission in 36% of intervention participants.[20,21] A significant reduction in body weight, especially greater than 15 kg compared to baseline, was highly predictive of remission of T2D.[20,23] Modest weight loss (10%) has been associated with impressive glycemic control and improvement in blood pressure and lipids.[24] Among participants in a 26-day residential program adhering to a high-fiber, low-cholesterol, low-salt, low-fat (<10% of energy) primarily plant-predominant diet combined with exercise, fasting blood glucose, total cholesterol, triglycerides, blood pressure (systolic and diastolic), and body weight were significantly reduced. Specifically, fasting glucose was lowered to <7.84 mmol/L in 76% of participants without medication use at program start.[25] The current study differs from this previous work, however, in its objective of examining remission using a plant-predominant diet without calorie restriction or fasting.

Also of note is an observed decrease in glucose-lowering medications following lifestyle change. Medication de-escalation or deprescribing is a planned process, supervised by the physician, by which medications are reduced or discontinued when no longer benefiting the patient.[26] The reduction in medication observed in this case series is similar to that described in a case series of practitioner protocols by Bradley et al[27] illustrating the reduced need for glucose-lowering medications following lifestyle intervention for T2D.

A nutritional approach to prevent diabetes has been long recognized by endocrine societies.[28,29] Moreover, adherence to a vegetarian diet is associated with better glycemic control.[30] In the Adventist Health Study-2, risk of T2D was lower among more plant-predominant diet followers (vegans, lacto-ovo, pesco-, and semi-vegetarians) as compared to nonvegetarians when adjusted for potential lifestyle confounders.[31] A variety of potential mechanisms driving these benefits have been explored, as plant-predominant diets may improve immunity, reduce inflammation, and reduce oxidative stress.[32-37] Plant-predominant diets may also mechanistically contribute to the reversal of insulin resistance.[38] These diets are typically lower in fat, high in fiber, nutrient-dense, and rich in whole grains, in addition to the presence of bioactive nutrient molecules (vitamins, minerals, fiber, etc.) and non-nutritive phytochemicals (phenolic compounds, flavonoids, and other bioactive peptides).

A high-fiber diet has multiple positive health effects, including reduced incidence of stroke, coronary heart disease, T2D, and colorectal cancer, as well as decreased mortality, body weight, systolic blood pressure, and cholesterol.[39] Significant beneficial effects on glucose homeostasis and insulin secretion have been found in populations with diabetes who increased their dietary fiber intake to 50 g per day (25 g soluble and 25 g insoluble fiber).[40] Furthermore, fiber nutritionally supports the vast intestinal anaerobic microbes which by fermentation produce health-promoting short-chain fatty acids (SCFA).[41,42] A whole-grain, high-fiber diet may improve insulin sensitivity and, thus, reduce risk of T2D.[43] In addition, the consumption of whole grains and legumes are known to reduce postprandial blood glucose, not only at the meal which they were consumed but also at subsequent meals which has important implications for day-long blood glucose control and prevention of diabetes.[44]

Short-chain fatty acids are byproducts of carbohydrate fermentation by the gut microbiota, and low SCFA production has been linked to T2D.[45] A 2018 randomized clinical study demonstrated that dietary fibers promote certain SCFA that yield improvements in metabolic outcomes such as HbA1c, whereby targeting improvements in production of these SCFAs may potentially help in improving T2D outcomes.[45]

A novel contribution of this study is the presentation of success cases from among a patient population not necessarily predisposed towards lifestyle change. Few patients in this practice intentionally sought out lifestyle treatment, highlighting the need for future research to quantify the proportion of patients with T2D who would be willing to undergo lifestyle treatment as part of routine

care, if invited to do so. While the proportion of patients willing to engage in lifestyle treatment was not systematically tracked in the EHR and, thus, cannot be determined for the purpose of this case series, these data indicate that patients are willing to engage in lifestyle change. Clinically, there are no identifiable drawbacks to presenting lifestyle interventions to all patients. Rather than assuming that patients may not be interested in changing health behaviors, a brief discussion encouraging a patient to consider lifestyle change may facilitate either more in-depth discussion and/or improved quality of life for a number of patients. Despite perceptions that plant-predominant diets may not be accepted by patients, research has shown that adherence to such a diet is feasible[46,47] with some studies reporting over 50% adherence.[19,22]

Remission of T2D has emerged as a therapeutic goal in T2D management, and achieving remission of T2D is a meaningful achievement in enhancing quality of life.[14,48] Furthermore, the opportunity to discontinue pharmacological treatment would eliminate its potential negative side effects.[49-52] While full remission may not be possible for all patients, improved glucose control without additional medications, or de-escalation of medications has beneficial implications. Patients deserve to be made aware that diabetes remission is possible through the adoption of an appropriately dosed, therapeutic lifestyle change.[14,48] A total of n = 22 (37.3%) patients in this case series achieved remission of T2D. The DIRECT Trial yielded 35.6% remission at 24 months post-intervention using the criteria of HbA1c < 48 mmol/mol (6.5%) following elimination of anti-diabetes medications at baseline.[20]

Aggressive, pharmacological blood glucose control over the long-term shows promising results in preventing cardiovascular events.[53,54] However, maintaining long-term tight glucose control requires continuous medical supervision and support from healthcare providers through a personalized approach,[14] while aggressive medical management with drug escalation may be accompanied by hypoglycemia and weight gain.[54]

In the present study, the prescription to adopt a plant-predominant diet may have contributed simultaneously to the decrease in BMI, fasting glucose, and HbA1c, as well as the reduction in the use of medications (insulin and oral glucose-lowering medications). This is consistent with previous research that has found weight loss to accompany improved glucose control.[20] To counter the legacy effect of diabetes (hyperglycemia) does not seem to be altogether hopeless. On the other hand, if a plant-predominant diet can be adopted early and followed long-term in this vulnerable group of patients, there may be an expected reduction in cardiovascular morbidity and mortality.

The strengths of this study include a relatively large sample size for a lifestyle intervention clinical case series, coupled with the fact that the patients were not from a self-selected sample and did not necessarily aim to seek out lifestyle treatment, but rather were steered in that direction *as part of routine care*. The primary limitation of this study is that no comparison or control group was possible, data on adherence was not available in the EHR, and the results may not be generalizable to other patients in the wellness clinic or in other healthcare settings. However, similar results with respect to improvements in diabetes outcomes and reduction in HbA1c and reduced need for medications following a plant-predominant diet treatment intervention have been observed by the author (G.P.) in this population.[13,55] It is also worth noting that this study did not collect nutrient intake data and although calorie restriction was not prescribed, it may have occurred indirectly as dietary patterns improved. Overall, this study supports the feasibility of improving glucose control, reducing glucose-lowering medications, and achieving remission of T2D among patients eating a predominantly low-fat, whole food, plant-predominant diet.

In conclusion, a lifestyle-based treatment intervention, predominately focused on education about the benefits of a plant-predominant diet for diabetes treatment and remission, resulted in decreased fasting blood glucose and HbA1c to a level achieving reduction of medications and remission of T2D. This study highlights the promising potential for a plant-predominant diet to confer immediate and long-term benefits with reduction of microvascular and macrovascular complications. These findings support the need for future research on the methods of provider and patient education in the application on lifestyle medicine principles and plant-predominant diet interventions in achieving diabetes remission, as well as measurement of the proportion of patients in typical medical practices that are willing to consider lifestyle changes as part of treatment. Future research should prospectively examine the factors leading to successful implementation of a plant-predominant diet intervention in achieving diabetes *remission* in every day medical practice and its long-term benefits.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr. Panigrahi and Ms. Goodwin are employees of the Wellness Clinic described in the manuscript. Dr. Karlsen and Ms. Staffier are employees of the American College of Lifestyle Medicine.

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Ethical Approval

This study was reviewed by the University of New England Institutional Review Board.

ORCID iDs

Kara Livingston Staffier https://orcid.org/0000-0003-0998-1178
Micaela Karlsen https://orcid.org/0000-0002-9365-151X AJLM

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