Plant-based Diet for HbA1c Reduction in Type 2 Diabetes Mellitus: an Evidence-based Case Report

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ABSTRAK

Latar belakang: diabetes telah menjadi salah satu masalah kesehatan utama di masyarakat dengan perkiraan jumlah 180 juta kasus di seluruh dunia. Pengelolaan nutrisi merupakan salah satu aspek penting dalam tatalaksana diabetes melitus tipe 2. Beberapa penelitian telah menunjukkan bahwa terdapat hubungan antara diet nabati dan perbaikan kontrol glikemik pada diabetes melitus tipe 2, namun hubungan tersebut masih belum dapat disimpulkan. Tujuan artikel ini adalah melakukan penilaian kritis untuk menganalisis apakah diet nabati dapat mengurangi kadar HbA1c dibandingkan dengan diet konvensional. Metode: penelusuran literatur menggunakan PubMed, Ovid, EBSCO, dan Cochrane Library. Semua abstrak dan judul dari hasil pencarian awal disaring dan hasil pencarian akhir ditelaah dengan kritis menggunakan lembar kerja penilaian Center of Evidence-Based Medicine, University of Oxford. Hasil: satu tinjauan sistematis dan dua uji klinis memenuhi kriteria inklusi dan dianggap memenuhi syarat untuk diikutsertakan dalam laporan kasus ini. Pada pasien dengan diabetes melitus tipe 2, HbA1c secara signifikan mengalami penurunan lebih besar pada kelompok diet nabati dibandingkan dengan kelompok diet konvensional setelah 22 minggu. Selain itu, terdapat penurunan yang lebih besar secara signifikan terhadap kadar HbA1c pada kelompok dengan diet nabati setelah 72 minggu. Berdasarkan hasil yang diperoleh, konsumsi diet nabati memiliki hubungan yang signifikan terhadap penurunan HbA1c. Kesimpulan: pada pasien dengan diabetes melitus tipe 2, penurunan kadar HbA1c lebih tinggi pada pasien dengan diet nabati dibandingkan dengan pasien dengan diet konvensional. Untuk penelitian selanjutnya sebaiknya dilakukan dengan menggunakan jumlah sampel yang lebih besar dan waktu tindak lanjut yang lebih panjang.

Kata kunci: tipe 2 diabetes melitus, diet, vegan, vegetarian, glukosa, HbA1c.

ABSTRACT

Background: diabetes has become a major public health concern with an estimated 180 million cases worldwide. Nutritional adjustment is one of the key aspects in the management of type 2 diabetes mellitus. Previous studies have suggested an association between vegetarian diets and improvements in glycemic control in type 2 diabetes mellitus, however the relationship is not well established. The aim of this report is to perform a critical appraisal to analyze whether plant-based diet reduces the HbA1c level compared to conventional diet. Methods: a comprehensive computer-based literature search was performed on June 20, 2016 using PubMed, Ovid, EBSCO, and the Cochrane Library. All abstracts and titles from the initial search results were screened, reviewed, and appraised using critical appraisal worksheets by Center of Evidence-Based Medicine, University of Oxford. Results: one systematic review and two RCTs met the inclusion criteria and were considered eligible for this case report. In patients with type 2 diabetes mellitus, HbA1c significantly yielded greater reduction in

the plant-based group compared to conventional diet group after 22 weeks of follow up. Similarly, there was a statistically greater reduction in HbA1c level in the plant-based group after 72 weeks. Furthermore, consumption of plant-based diet was associated with a significant reduction in HbA1c. **Conclusion:** *in patients with type 2 diabetes mellitus, HbA1c reduction was greater in patients with plant-based diet compared to patients with conventional diet. Further research should be conducted with larger sample size and longer follow-up period.*

Keywords: diabetes mellitus, type 2, diet, vegans, glucose, HbA1c.

INTRODUCTION

Diabetes has become a major public health concern with an estimated 180 million cases worldwide.[1] The number of people worldwide with type 2 diabetes mellitus is expected to double by 2030.[2] In Indonesia, based on the data from RISKESDAS 2013 (Riset Kesehatan Dasar), it was estimated that the proportion of Indonesian population ≥15 years of age with type 2 diabetes mellitus is 6.9%.[3] Based on the data by IDF (International Diabetes Federation) in 2014, Indonesia ranked fifth among countries with the highest proportion of type 2 diabetes mellitus. This is a setback compared to the 2013 data, in which Indonesia was placed on the seventh position. The problem in Indonesia is that not all patients are able to get adequate access to healthcare. There is also lack of availability of oral hypoglycemic drugs in primary healthcare center (Puskesmas) as well as other healthcare centers. In addition, there is lack of ability among healthcare providers in managing diabetes cases, specifically in preventive, curative, and rehabilitative aspects.[4]

Nutritional adjustment is one of the key aspects in the management of type 2 diabetes mellitus. The main principle of nutritional management of type 2 diabetes is hypocaloric diet, which is low in calories.[5] The dietary approaches for managing type 2 diabetes include limiting carbohydrate intake, limiting intake of saturated and trans fats and cholesterol, and reducing energy intake in overweight individuals. However, one of the major problems with conventional hypocaloric diet is poor long-term patient adherence. Alternatively, vegetarian or plant-based diet may be a convenient strategy to encourage consumption of foods with a lower energy density.[6]

Vegetarian diets are characterized by elimination of all flesh foods from the diet and typically based on the consumption of whole grains, legumes, vegetables, fruits, and nuts, while still consuming eggs and dairy products like milk and butter. On the other hand, the term vegan refers to diets contain only plant foods. In randomized trials, vegetarian and low-fat vegan diets have been shown to improve glycemic control, blood lipid concentrations, and body weight compared to conventional dietary guideline, which includes the consumption of animal products.[6] These improvements may be due to the fact that individuals who adhere to plant-based eating pattern typically consume fewer calories and less fat, saturated fat, and cholesterol and consume more fiber, potassium, and vitamin C. Recently, both the American Academy of Nutrition and Dietetics and the American Diabetes Association (ADA) included well-planned, plant-based eating patterns (vegetarian and vegan) as a nutritional intervention in their recommendations for people with diabetes.[7]

Previous studies have found that plant-based eating patterns combined with exercise have been found to improve diabetes control and reduce the need for medication. Specifically, several studies have suggested an association between vegetarian diets and improvements in glycemic control in type 2 diabetes mellitus, however the relationship is not well established.[7] As a result, it is timely to advise an effective dietary plan to contribute to an overall management plan for patients with type 2 diabetes mellitus, especially for those who are unable to afford flesh foods in their daily dietary regiment.

CLINICAL QUESTION

A 51-year-old female came to the clinic for routine control for type 2 diabetes mellitus. She was diagnosed with type 2 diabetes mellitus

since 1 year ago. Patient was worried because her blood glucose levels were still high. She also complained of pain and tingling sensations on her both feet since 1 month ago. Due to this complaint, patient was unable to work, therefore she could not help her husband as the breadwinner in the family.

Patient was diagnosed with type 2 diabetes mellitus in 2015 when she went to the clinic with the chief complaint of fatigue. In addition, patient also complained of excessive thirst, excessive hunger, and nocturnal urination. Laboratory examinations for her glucose level were conducted and the result showed that her random blood glucose level was approximately 500 and she was asked to return to the clinic the next morning to check for her fasting blood glucose and post prandial glucose. The tests showed that the patient's fasting blood glucose was 271, while the postprandial glucose was 441. Patient was given two oral hypoglycemic agents which are Metformin and Glibenclamid and she was asked to come to the clinic the following month for routine control. However, patient used to skip her routine control schedule and there was a time when she did not consume oral hypoglycemic drugs. Upon physical examination, vital signs were within normal limits. Examination of eyes, lungs, cardiovascular, and abdomen were also within normal limits. However, the touch sensitivity test revealed that there was loss of sensitivity on the plantar side of both feet.

The latest blood glucose measurements of this patient was 243 mg/dl for fasting blood glucose and 506 mg/dl for postprandial. Patient's HbA1c level was 8.2%, which is above the target for patients with diabetes mellitus. Patient was given three oral hypoglycemic agents, with the addition of Acarbose into the regiment. In addition medications, patient was also advised to do physical activity and diet modifications. Patient came from low socio-economic background and was unable to afford buying flesh foods for protein such as meat and chicken on a regular basis. Patient usually ate plant-based foods such as white rice with vegetables, tofu (tahu), tempeh, crackers, and sometimes alternated with eggs or fish.

The clinical question for this EBCR is: "In patients with type 2 diabetes mellitus, does plant-based diet reduce the HbA1c level compared to conventional diet?"

METHODS

In order to answer the clinical question, a comprehensive computer-based literature search was performed on June 20, 2016 using PubMed, Ovid, EBSCO, and the Cochrane Library. The searching process used combinations of Boolean operators such as 'AND' and 'OR' and the following key words: 'plant-based', 'vegetarian', 'vegan', 'diet', 'diabetes', 'HbA1c', and 'glucose'. Limits placed on the search included 'English', 'humans', 'full text available', 'clinical trial', 'review', and 'articles published in the last ten years (June 2006 – June 2016)'. Several searches were conducted in order to ensure that all the relevant trials were identified. All abstracts and title from the initial search results were screened and reviewed in order to confirm that they fulfilled the inclusion and exclusion criteria. All relevant studies were appraised using critical appraisal worksheets by Center of Evidence-Based Medicine, University of Oxford.

RESULTS

A total of twelve studies were retrieved after the abstract and title screening process in a comprehensive computer-based literature search (**Figure 1**). After reading the full-text version of the studies, four articles were removed due to the irrelevance to the topic. In total, there are three articles used in this case report. All of the studies were appraised using the criteria from Centre of Evidence-Based Medicine University of Oxford for randomized clinical trial (RCT) and systematic review. (**Table 1**)

The study by Barnard et al.[8] investigated whether a low-fat vegan diet improves glycemic control and cardiovascular risk factors in individuals with type 2 diabetes. Individuals with type 2 diabetes were randomly assigned to a low-fat vegan diet or a diet following the American Diabetes Association (ADA) guidelines and evaluated at the start of the trial and at 22 weeks. The vegan diet consisted of vegetables, fruits,
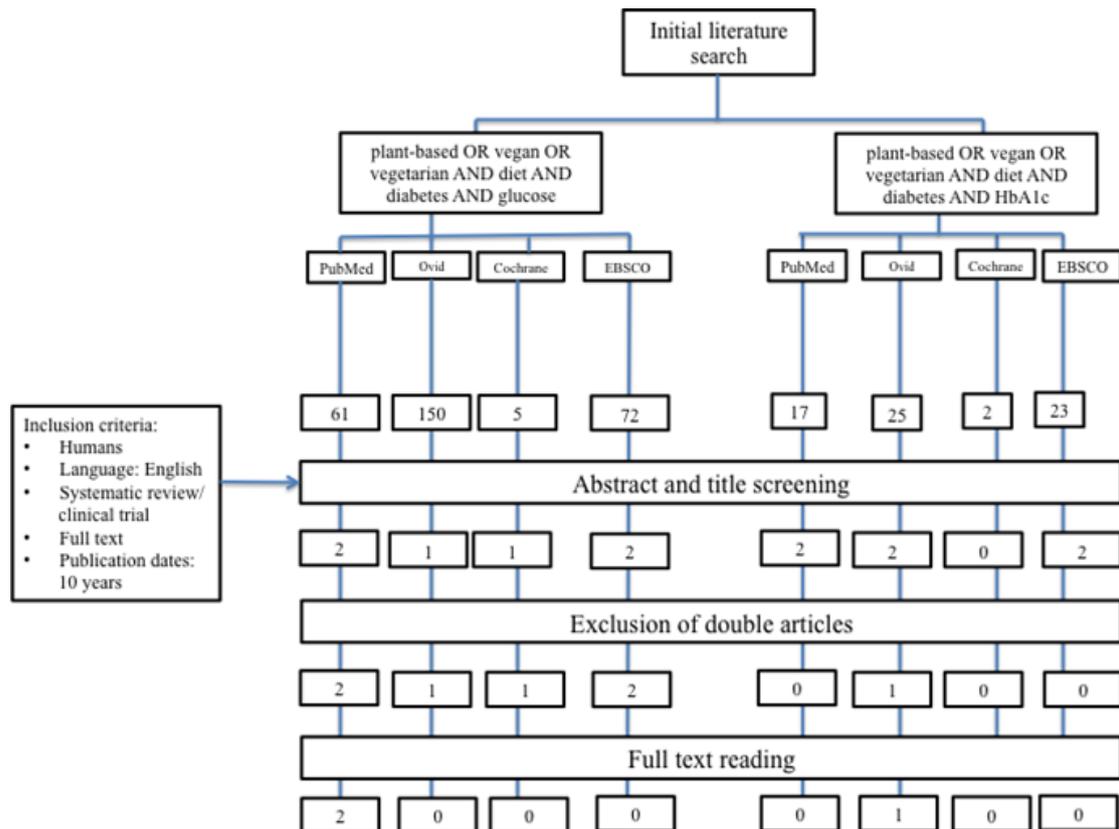
Figure 1. Flowchart of the searching and selection strategy

grains, and legumes and participants were asked to avoid animal products while the control group was assigned to the ADA diet. The outcomes assessed in this study include anthropometric and glycemic variables, renal variables, and lipid profiles. Glycemic variables include HbA1c which is measured in percentage (%), fasting plasma glucose, measured in mmol/l, and fasting plasma glucose , measured in mg/dl.

In all participants, HbA1c fell 0.96 percentage points (p=0.0001) in the vegan group and 0.56 percentage points (p=0.0009) in the ADA group. In participants whose diabetes medications remained unchanged throughout the trial (24 participants in the vegan group and 33 participants in the ADA group, HbA1c fell 1.23 points in the vegan group and 0.38 points in the ADA group and this result is statistically significant (p=0.01; baseline-adjusted p=0.007). As for the fasting blood glucose in mmol/l, the mean blood glucose level decreased by 1.97 mmol/l in the vegan group and 1.92 mmol/l in

the ADA group. However, these results are not statistically significant (p=0.92). A similar trend was also observed in the fasting blood glucose in mg/dl, in which the mean decrease was higher in the vegan group with 35.5 mg/dl compared to the ADA group 34.6 mg/dl. However, these results were not statistically significant (p=0.92). Based on the results of glycemic markers and lipid profiles, it was shown that both a low-fat vegan diet and a diet based on ADA guidelines showed improvement, however the improvements were greater with a low-fat vegan diet.

The second study was conducted by the same principal authors, Barnard et al.[9]. However this study was conducted three years after the first study with a longer follow-up period, which was up to 74 weeks. Similar with the previous study, this study also compared the effects of a low-fat vegan diet and conventional diabetes diet on glycemic markers, weight, and plasma lipids. The study design was also similar, in which individuals with type 2 diabetes were randomly

Table 1. Critical appraisal of the included randomized controlled trials based on criteria by Centre of Evidence Medicine University of Oxford

| Articles | PICO | Validity | | | | | Results | | | Level of evidence |
		Was the assignment of patients to treatments randomized?	Were the groups similar at the start of the trial?	Were groups treated equally?	Were all patients who entered the trial accounted for? – and were they analyzed in the groups to which they were randomized?	Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?	How large was the treatment effect?	How precise was the estimate of the treatment effect?	Study results	
Bernard et al.[8]	+	Yes	Yes	Yes	Yes	Not blinded	Effect size (mean (SE)): -0.4 (-0.9 to 0.1)	p=0.09	A	1B
Bernard et al.[9]	+	Yes	Yes	Yes	Yes	Not blinded	Effect size (mean ±SE): -0.41 (-0.78 to -0.04)	p=0.03	B	1B

+ stated clearly in the article; - not being done; ? not stated clearly

A. In all participants, HbA1c decreased 0.96 percentage points in the vegan group and 0.56 points in the ADA group (P=0.089). Excluding those who changed medications, HbA1c decreased 1.23 points in the vegan group compared with 0.38 points in the ADA group (P= 0.01). B. In all participants, HbA1c changes from baseline to 74 week or last available values were -0.34 and -0.14 for vegan and conventional diets, respectively (P=0.43). HbA1c changes from baseline to last available value or last value before any medication adjustment were -0.40 and 0.01 for vegan and conventional diets, respectively (p=0.03)

assigned to a low-fat vegan diet or a diet following 2003 American Diabetes Association guidelines or conventional diet for 74 weeks.

The glycemic markers analyzed in this study are HbA1c and fasting plasma glucose in mg/dl. For HbA1c, the repeated-measures analysis of variance showed significant effects for time (p<0.0001) and for diet group-by-time interaction (p=0.03). In an intention-to-treat analysis which includes all participants, HbA1c changes from baseline to 74 week or to the last available value were -0.34 for the vegan group and - 0.14 for the conventional diet group, however this result is not statistically significant (P=0.43). The decrease in mean fasting plasma glucose was also higher in the vegan group (19.5 mg/dl) compared to the ADA group (14.0 mg/dl), however this result is not statistically significant (P=0.61). Similar with the previous study, this study also concludes that, a low-fat vegan diet appeared to improve glycemia and plasma lipids more than conventional diabetes diet.

The third study is a systematic review and meta-analysis by Yokoyama et al.[10] which emphasizes on the associations between vegetarian diets and glycemic control in type 2 diabetes. The studies included in this review are clinical trials in adults in which vegetarian diets (defined as those excluding meat, poultry, and fish) or vegan diets (defined as excluding animal-derived food products) were used as interventions for at least 4 weeks and changes in HbA1c and/ or fasting blood glucose levels were reported. The main measure of interest was the HbA1c level in patients consuming vegetarian or vegan diets, compared with levels in patients in the control group (omnivorous diet), while the secondary endpoint was the change in the fasting blood glucose level. A comprehensive literature search was conducted in PubMed, Web of Science, EMBASE, and the Cochrane Central Register of Controlled Trials. In total, there were six studies included in this review.

The result of this review revealed that consumption of vegetarian diets was associated with a significant reduction in HbA1c [−0.39 percentage point; 95% confidence interval (CI), −0.62 to −0.15; P=0.001; I2=3.0; P for heterogeneity =0.389]. On the other hand, there

was a non-significant reduction in fasting blood glucose concentration (−0.36 mmol/L; 95% CI, −1.04 to 0.32; P=0.301; I2=0; P for heterogeneity =0.710), compared with consumption of omnivorous diet.

DISCUSSION

Prior research has demonstrated that a low-fat, plant-based nutritional approach improves control of weight, glycemia, and cardiovascular risk in type 2 diabetes patients.[11] In addition, studies have reported a dramatic decrease in medication use when following a plant-based diet. These results are in accordance with studies included in this case report in which HbA1c as the glycemic marker shows a greater decrease in the vegan group compared to the ADA group. In addition, the study by Barnard et al.[8] also found that more patients in the vegan group (43% percent or 21 of 49) reduced diabetes medications compared to the ADA group (26% or 13 of 50). This is due to the fact that a low-fat plant-based diet plays an important role in nutrient intake and body composition in several ways that may affect insulin sensitivity. The underlying mechanism is that those types of diets are low in fat and high in fiber, therefore typically cause associated reductions in dietary energy density and energy intake, which are not fully compensated for by increased food intake. In addition, weight-reducing effect of the vegan diet is found to be responsible for a significant portion of its effect on HbA1c.[6]

The second study by Barnard et al.[9] has longer follow up-period compared to the first study from the same author. It was shown that the result was also the same after long- term follow up (74 weeks), in which there was a significantly greater decrease in HbA1c changes from baseline to week 74 in vegan diet group. However, among participants in the vegan group with no changes to diabetes medications, HbA1c had fallen 1.23 by 22 week (n=24) and 0.82 by 74 week (n=14), meaning that the decrease was greater in week 22 compared to week 74. Among the conventional diet group, the similar trend was also observed, in which HbA1c reduction was greater at week 22 compared to week 74 (0.38 with n=33 and 0.21 with n=21, respectively). These results are in

accordance to the previous study which implied that long-term effect of both diet interventions on glycemia was reduced in comparison with the short-term findings from this study.[8] However, in both studies by Barnard et al.[9], participants were not blinded to the intervention due to the obvious differences between the diets, thus making the results prone to bias. In addition, most participants in both groups altered medications due to low blood glucose values, therefore presenting a confounding variable that required special analyses.

The systematic review by Yokoyama et al.[10] also found that consumption of vegetarian diets was associated with a significant reduction in HbA1c. The meta-analysis revealed that a vegetarian dietary pattern significantly reduced HbA1c by 0.4 percentage point in patients with type 2 diabetes. The magnitude of the effect size is roughly one-half of that seen with metformin, which is used as first-line oral therapy for elevated HbA1c levels. On the other hand, the reductions seen in fasting blood glucose level did not reach statistical significance. One of the strengths of this review is that there was no significant heterogeneity among the controlled trials included in the analysis. However, several drawbacks of this review are the fact that trials included in this review have small sample sizes and some of the studies included in the review were not randomized.

Based on the study by Selvin et al.[12] this issue may be caused by the fact that glucose levels are often variable while baseline HbA1c level is a stronger predictor of subsequent diabetes and cardiovascular events than fasting glucose. Moreover, in clinical practice, HbA1c is widely used in diabetes care as a reliable marker of long- term glycemic control.[13] However, since HbA1c refers to glycosylated hemoglobin, which is developed when glucose attaches to the hemoglobin in the red blood cell, HbA1c is unable to be used for evaluation purpose in certain cases such as anemia, hemoglobinopathy, history of blood transfusion within 2-3 months, and other conditions which may affect erythrocyte life cycle and kidney function.[4]

In this case, the level of HbA1c of the patient is 8.2%, which is still above the target for type 2 diabetes mellitus control. Based on the meta-analysis, the vegetarian dietary pattern only reduced HbA1c level by 0.4 percentage point.[10] On the other hand, the target HbA1c level as written in the criteria for type 2 diabetes mellitus control is below 7%. As a result, it is still inadequate to rely solely on the diet to decrease the HbA1c level to reach the controlled level as the management of type 2 diabetes mellitus. The patient requires aggressive treatment in the form of oral antidiabetic agents (OAD) to achieve glycemic and cardiovascular risk factor goals. According to the meta-analysis by Sherifall et al.,[14] the benefit of initiating an OAD agent can be seen within the first 4 to 6 months of administration, with HbA1c levels reduction by up to 1.5% on average. Therefore, the administration of OAD agent and plant-based dietary pattern should be applied simultaneously to achieve the desired HbA1c level.

CONCLUSION

Based on the results and discussion of the included studies, it is concluded that in patients with type 2 diabetes mellitus, HbA1c reduction was greater in patients with plant-based diet compared to patients with conventional diet.

In patients with type 2 diabetes mellitus, fasting blood glucose reduction was greater in patients with plant-based diet compared to patients with conventional diet.

Further research with larger sample size and extensive follow-up period is needed to establish a firm conclusion regarding this issue. In addition, further studies are needed to investigate the relationships between specific foods, preferably foods which are commonly consumed in the society, and glycemic control.

In clinical settings, fasting blood glucose is more commonly used for glycemic control due to its availability and practicality. Based on the recent consensus by PERKENI, HbA1c should be examined every 3 months or each month for cases with high level of HbA1c (>10%). Moreover, HbA1c is an excellent marker for long-term monitoring for type 2 diabetes mellitus. However, because of the lack of availability and practicality of HbA1c examination, further research with fasting blood glucose as the

main outcome should be conducted due to the relevance with the clinical settings.

In terms of clinical implementation in this patient, along with medications and other lifestyle modifications such as exercise, the patient should be advised to continue her dietary pattern that includes plant-based foods which are rich in vegetables, fruits, grains, and legumes. However, the patient should be educated in regards to the portion size in order to ensure that patient gets adequate energy intake and micronutrient, especially for sources of vitamin B-12, vitamin D, and calcium.

ACKNOWLEDGMENTS AND AFFILIATIONS

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