

The effect of walnut consumption on lipid profiles of the first-degree relatives of type two diabetes mellitus patients (T2DM) with prediabetes

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ABSTRACT

Background and Objective: Prevalence of Diabetes mellitus as a group of metabolic diseases is increasing. Abnormal lipid profile in diabetic patients is major risk factor for cardiovascular disease. According to studies, polyunsaturated fatty acid (PUFA) effect on lipid profile. We evaluated the association between walnut consumption as a source of PUFA and high-density lipoprotein cholesterol (HDL-C) in prediabetic patients.

Methodology: Four hundred eleven (411) first-degree relatives of T2DM male and female 35 to 55 year of age were included in the present study. Dietary intake was assessed with three days record and record's contents were changed to grams. Biochemical assessments were done according to the standard protocol.

Results: Findings show positive associations between walnut consumption and HDL-C level ($p=0.01$). No other significant associations were observed between other blood lipid components, glycemic control parameters and walnut consumption.

Conclusions: Walnut consumption may improve HDL-C in prediabetes patients who were the first-degree relatives of type two diabetic patients.

KEY WORDS: Walnut, Blood lipids, Prediabetic state.

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INTRODUCTION

Diabetes mellitus as a group of metabolic diseases is characterized by hyperglycemia resulting from insulin resistance and beta cell dysfunction.¹ The prevalence of diabetes has increased over the past and was estimated to increase further by 50% in the world by the year 2030.² Blindness, kidney failure, limb amputation and cardiovascular disease are major complication of diabetes.³ Sedentary lifestyle, obesity and changing diet toward processed foods, have been related to rise in diabetes prevalence.⁴ Abnormal lipid profile in diabetic patients is major risk factor for cardiovascular disease. Studies have showed that diet with low saturated fatty acids contents decrease low density lipoprotein cholesterol (LDL-C) levels and cardiovascular events.⁵ It also showed that replacing saturated

and trans fatty acids with unsaturated fatty acids, including nuts in diet, may help to prevent from diabetes.⁶ Nuts have some components like fiber and magnesium that decrease insulin resistance.⁷⁻¹⁴ Walnut has a higher content of polyunsaturated fatty acid (PUFA) and alpha-linolenic acid.

PUFA reduced LDL-cholesterol and total cholesterol.¹⁵ Some studies have showed that walnut decrease total cholesterol and LDL-C and increase high-d have recommended that walnut consumption protect against cardiovascular disease.^{21,22} Most of studies were done on type 2 diabetes mellitus (T2DM) patients. Literature search showed that there was no study that evaluated the effect of walnut consumption on pre-diabetes patients who were the first-degree relatives of T2DM patients. In this study, we evaluated the role of walnut consumption on lipid profiles in pre diabetes patients who were the first-degree relatives of T2DM patients.

METHODOLOGY

Participants: This was a cross-sectional study. The participants were the first-degree relatives of T2DM people in Isfahan Diabetes Prevention Study (IDPS). Our aim in IDPS was to prevent from T2DM by changing life style or by medication intervention among at high-risk group. We selected participants from a cohort study that was conducted from 2003 until now with 3454 member in Isfahan Endocrine and Metabolism Research Center (IEMRC). One thousand fifty member had food record. Diabetic patient (n=46) and patient with normal glucose tolerance test (n=364) excluded from study. From 640 pre diabetics 229 subjects did not report walnut consumption in their records. Finally, 411 men and female 35 to 55 year of age were included to this study. Those who use medicine that effect on glucose tolerance test and lipid profiles were excluded. Pre diabetes patients according to ADA criteria²³ (23) included impaired fasting glucose (IFG), those with fasting blood glucose 100-125 mg/dl (n=48) and Impaired Glucose Tolerance (IGT), blood glucose 120 minute after intake 75gr oral glucose, 140-199 mg/dl, (n=53) and combined pre diabetics, IFG +IGT (n=310) were include. The Isfahan Endocrine and Metabolism Research Center (IEMRC) Medical Ethics Committee approved this study and each participant written informed consent.

Assessment of dietary intake: Dietary intake was assessed by use of three days record and trained dietitian adjusted it. These records had eleven columns that included cereals group, legumes,

dairy, meat, fat, nuts, and fruit, vegetable, sweet, sugar, and drinks. Dietitians educated groups how to prepare records. Then record's contents were changed to grams.²⁴ Weight of each walnut was considered 4 grams.

Anthropometric assessment: Weight was measured by Seca (Germany) scale while subject were lightly clothed and without shoes and recorded to the nearest 100 gr. Height was measured by Seca stadiometer while subjects were in a standing position with their shoulders in normal position. Body mass index was computed as weight (kilograms) divided by height (meters) squared.

Biochemical assessment: Blood samples were taken from 7:30 to 9:30 AM, after 12 hour overnight fasting to determine serum lipids and whole blood glucose levels. Blood glucose, serum triglyceride (TG), total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels were determined by using an enzymatic method. Oral Glucose Tolerance Test (OGTT) was done after 10-12 hours of overnight fasting, a 75 gr oral glucose was administered and plasma glucose concentrations were measured at fasting and 120 minutes after glucose taking (BS120). The analysis of sample was performed with an auto analyzer (BT 3000, Rome, Italy) using commercial kits (Chem Enzyme, Tehran Iran). Serum total cholesterol and triglycerides levels were measured by enzymatic reagents (Chem. Enzyme, Tehran Iran) adapted to Selecta auto analyzer.

HDL-C levels were measured by using available commercial kits (Pars Azmun, Tehran Iran). Low density lipoprotein cholesterol levels (LDL-C) were calculated from the values of serum triglyceride (TG), total cholesterol and HDL cholesterol according to the Fried Wald formula in triglyceride <400 mg/dl:²⁵ $LDL-C = Total\ cholesterol - HDL-C - (TG/5)$ HbA1c were assessed with DS5 analyzer uses low pressure cat ion exchange chromatography in conjunction with gradient elution to separate human hemoglobin subtypes and variants from haemolysed whole blood.^{26,27}

Inter assay coefficients of variations were 1.25 for triglycerides, 1.2 for cholesterol and 1.25 for glucose. The corresponding intra-assay coefficients of variations were 1.97, 1.6 and 2.2, respectively.

Statistical analysis: SPSS (version 13) was used for statistical analysis. Continuous variables presented as mean \pm standard deviation. Partial correlations between continuous variables evaluated by Pearson's partial *r* coefficient, after adjusting for age, sex and BMI. The relationships between lipid profiles and glycemic control parameters

Table-I: Clinical and biochemical variables of participants.

Variables	Mean(SD)
Age	
SBP*	
DBP**	
WC***	
BMI(kg/m ²)	44.66 (6.7)
11.68 (1.6)	
7.58 (1.1)	
90.92 (9.4)	
30.23 (4.4)	
FBS (mg/dl)	109.62 (7.2)
BS120 (mg/dl)&	164.21(16.8)
HbA1C (%)	5.3 (0.8)
TG (mg/dl)	184.15 (23.1)
Total Cholesterol (mg/dl)	206.28 (31.2)
HDL-C (mg/dl)	44.84 (11.3)
LDL-C (mg/dl)	125.57 (33.1)
Walnut consumption	22.52 (8.4)
Energy intake (calorie)	1573.52 (519.4)
Total fat intake (g)	49.05 (20.5)

*systolic blood pressure, **diastolic blood pressure, ***waist circumference & Blood sugar120 minutes after glucose taking.

(dependent variable) with walnut consumption were examined using multiple linear regression analysis, after controlling for potential confounders (adjusted with age, sex, BMI, energy intake and total fat intake). $P < 0.05$ was considered statistically significant.

RESULTS

About 18% of participant were men and 82% were women. Clinical and characteristics of the study participant are shown in Table-I.

Table-II shows the partial correlation coefficients between walnut consumption and lipid profiles and glycemic control parameters. When we stratified

Table-II: Partial correlation coefficients between glycemic control parameters, lipid profiles and Walnut consumption after adjusting for age, sex and BMI.

Biochemical Variables	Walnut consumption
FBS (mg/dl)	0.089
BS120(mg/dl)*	0.159
HbA1C (%)	-0.039
TG (mg/dl)	0.037
Total Cholesterol (mg/dl)	0.103
HDL-C (mg/dl)	0.227**
LDL-C(mg/dl)	0.019

* Blood sugar120 minutes after glucose taking, ** $p < 0.05$

the analysis by gender, no gender differences were observed in the magnitude of the correlations of Walnut consumption and lipid profiles and glycemic control parameters. Thus, the analysis was performed after adjusting with age, sex and BMI. Walnut consumption was positively correlated with HDL-C levels but not with glycemic control parameters and other lipid profile components.

Relationships between lipid profiles and glycemic control parameters with walnut consumption may be confounded by several characteristics, especially dietary habits and obesity. Thus, we applied multiple regression analysis (Table-III) and after controlling for total energy and total fat intake, body mass index, sex and age we found positive associations between walnut consumption and HDL-C level ($p = 0.01$). No other significant associations were observed between other blood lipids, glycemic control parameters and walnut consumption.

DISCUSSION

In this, study walnut consumption affected on HDL-C levels and it could increase HDL-C levels but it did not have any effect on glycemic control parameters and other lipid profile components. A number of clinical trials have examined the

Table-III: Multiple regression analysis on the association between walnut consumption, lipid profiles and glycemic control parameters.

Lipid profiles and glycemic control parameters	R ²	B ± SE	P
Model 1: TG(mg/dl)	0.092	0.388 (0.420)	0.357
Model 2: Total cholesterol(mg/dl)	0.095	0.207 (0.156)	0.188
Model 3: HDL-C(mg/dl)	0.141	0.121 (0.047)	0.01
Model 4: LDL-C(mg/dl)	0.073	0.035 (0.138)	0.799
Model 5: FBS(mg/dl)	0.011	0.032 (0.031)	0.30
Model 6: BS120(mg/dl)	0.018	0.056 (0.072)	0.435
Model 7: HbA1c(%)	0.013	-0.003 (0.005)	0.545

Data are B-coefficient ± SE, Lipid profiles and glycemic control parameters are dependent, Values are corrected for various confounders such as total energy and total fat intake, body mass index, sex and age.

affect of walnut diet on serum lipids of patient with type two diabetes and their finding showed that diet supplementation with 30 g/d walnut significantly reduced LDL-C and increased HDL-C in these patients.²⁸ Kesavulu et al, reported that two months therapy with supplementation of 1.8 g/day n-3 long -chain polyunsaturated fatty acids (n-3 LC-PUFAs) in type two diabetes patients treated with antidiabetic drugs, significantly reduced TG levels and increased HDL-C levels without changing glycemic parameters.²⁹ On the other hand another study reported no significant effects of n-3 LC- PUFAs on LDL-C levels in subjects with type two diabetes.³⁰ Recent review study based on 13 randomized trials of type two diabetes patients showed n-3 LC- PUFAs reduce serum TG levels, but have no effect on total LDL-C or HDL-C levels.³¹ Another randomize study reported that diet containing 30 g walnut improve the lipid profiles in diabetic patients.²⁸ One meta-analysis found significant improvements in lipid profiles with high walnut consumption compared with various control diets. Despite their high fat content, walnut doesn't appear to adversely affect.³² A randomize trial study suggested that diet plus 30 g/d walnut increase HDL-C: Total cholesterol ratio, and decreased by 10% in plasma LDL-C in walnut group compare with the other group.³³ Other observations in contrast of our data suggested that nut including walnut reduce HDL-C levels.^{20,34} In our study consumption of walnut did not have any effect on glycemic control parameters. Studies done on type two diabetes didn't have demonstrated improvement in glycemic control after walnut consumption.^{28,35,36} According to our finding and other studies^{37,38} the affect of walnut in increasing HDL-C levels may be due to the fatty acid composition of walnut.²⁸ Walnut is one of the highest sources of alpha-linolenic acid (ALA). Recent studies have reported dietary intake of ALA has been inversely associated with risk of fatal coronary heart disease.^{39,40} ALA has antiatherogenic and antiarrhythmic properties.⁴¹

CONCLUSION

In conclusion, our study supports a positive association between walnut consumption and HDL-C in prediabetes patient who were the first-degree relative of type two diabetic patients. Lipid profiles disturbance are one of the complication of this and risk factor for cardiovascular disease, so walnut consumption may improve lipid profiles in prediabetes patients.

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REFERENCES

1. Ma Y, Njike V, Millet J, Dutta S, Doughty K, Treu J. Assessment of the effect of mixed nuts on glycemic control and coronary heart disease risk factors in type 2 diabetes. *Diabetes Care*. 2010;33:227-232.
2. Shaw J, Sicree R, Zimmet P. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract*. 2010;87(1):4-14.
3. Stratton I, Adler A, Neil H, Mathews H, Manley S, Cull C, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35) prospective observational study. *BMJ*. 2000;321(7258):405-412.
4. Kendall C, Esfahani A, Truanm J, Srichaikul K, Jenkins D. Health benefits of nuts in prevention and management of diabetes. *Asia Pacific J Clin Nutr*. 2010;19(1):110-116.
5. Ulbricht T, Southgate D. Coronary heart disease: seven dietary factors. *Lancet*. 1991;338:985-992.
6. Schulze M, Hu F. Primary prevention of diabetes: what can be done and how much can be prevented? *Ann Review Public Health*. 2005;26:445-467.
7. Anderson J, Gustafson N, Bryant C, Tietjen-Clark J. Dietary fiber and diabetes: a comprehensive review and practical application. *J Am Diet Assoc*. 1987;87:1189-1197.
8. Paolisso G, Scheen A, D'Onofrio F, Lefebvre P. Magnesium and glucose homeostasis. *Diabetologia*. 1990;33(9):511-514.
9. Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesaro P, Varricchio M, et al. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr*. 1992;55(6):1161-1167.
10. Paolisso G, Sgambato S, Pizza G, Passariello N, D'Onofrio F. Improved insulin response and action by chronic magnesium administration in aged NIDDM subjects. *Diabetes Care*. 1989;12:265-269.
11. Resnick L. Ionic basis of hypertension, insulin resistance, vascular disease, and related disorders: the mechanism of "syndrome X. *Am J Hypertens*. 1993;6(4):123S-134S.
12. Rivellesse A, Riccardi G, Giacco A, Pacioni D, Genovese S, Mattioli PL, et al. Effect of dietary fibre on glucose control and serum lipoproteins in diabetic patients. *Lancet*. 1980;2(8192):447-450.
13. Simpson HC, Simpson RW, Lousley S, Carter RD, Geekie M, Hockaday TD, et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet*. 1981;1(8210):1-5.
14. Sjogren A, Floren C, Nilsson A. Oral administration of magnesium hydroxide to subjects with insulin dependent diabetes mellitus: effects on magnesium and potassium levels and on insulin requirements. *Magnesium*. 1988;7:117-122.
15. Feldman E. The scientific evidence for a beneficial health relationship between walnuts and coronary heart disease. *J Nutr*. 2002;132:1062S-101S.

16. Abbey M, Noakes M, Belling G, Nestel P. Partial replacment of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol. *Am J Clin Nutr.* 1994;59:995-9.
17. Chisholm A, Mann J, Skeaff M, Frampton C, Sutherland W, Duncan A, et al. Adiet rich in walnuts favourably influences plasma fatty acid profile in moderately hyperlipidaemic subjects. *Eur J Clin Nutr.* 1998;52:12-16.
18. Lavedrine F, Zmiron D, Ravel A, Balducci F, Alary J. Blood cholesterol and walnut consumption:a cross-sectional surveyin France. *Prev Med.* 1999;28(4):333-339.
19. Sabate J, Fraser G, Burke k, Knutsen S, Bennett H, Lindsted K. Effects of walnuts on serum lipid levels and blood prssure in normal men. *N Engl J Med.* 1993;328:603-607.
20. Zambon D, Sabate J, Munoz S, Campero B, Casals E, Merlos M, et al. Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women. A randomized crossover trial. *Ann Intern Med.* 2000;132:538-546.
21. Fraser G, Sabate J, Beeson W, Strahan T. A possible protective effect of nut consumption on risk of coronary heart disease The Adventist Health Study. *Arch Intern Med.* 1992;152:1416-1424.
22. Tapsell L, Gillen L, Patch C. Walnuts and dietary approaches to the prevention and management of abnormal lipid profiles in Type2 diabetes mellitus. *Future Cardiology.* 2005;1:809-814.
23. Seino M, Nanjo K, Tajima N, Kadowaki T, Kashiwagi A, Araki E, et al. Report of the Committee on the Classification and Diagnostic Criteria of Diabetes Mellitus. *J Diabet Invest.* 2010; 1(5):212-228.
24. Ghafarpour M, Hosharrad A, Kianfar H. The manual for household measures, cooking yield factors and edible portion of foods. keshavarzi press, Tehran, 1999.
25. Bećarević M, Andrejević S, Miljić P, Bonaci-Nikolić B, Majkić-Singh N. Serum lipids and anti-oxidized LDL antibodies in primary antiphospholipid syndrome. *Clin Exp Rheumatol.* 2007;25(3):361-366.
26. Frank E, Moulton L, Little R, Wiedmeyer H, Rohlfing C, Roberts W. Effects of hemoglobin C and S traits on seven glycohemoglobin methods. *Clin Chem.* 2000;46:864-867.
27. Roberts W, De B, Brown D, Hanbury C, Hoyer J, John W, et al. Effects of hemoglobin C and S traits on eight glycohemoglobin methods. *Clin Chem.* 2002;48:383-385.
28. Tapsell L, Gillen L, Patch C, Batterham M, Owen A, Bare M, et al. Including walnuts in a low-fat/modified-fat diet improves HDL cholesterol-to-total cholesterol ratios in patients with type 2 diabetes. *Diabetes Care.* 2004; 27(12):2777-2783.
29. Kesavulu M, Kameswararao B, Apparao C, Kumar E, Harinarayan C. Effect of omega-3 fatty acids on lipid peroxidation and antioxidant enzyme status in type 2 diabetic patients. *Diabetes Metab.* 2002;28:20-26.
30. Woodman R, Mori T, Burke V, Puddey I, Watts G, Beilin L. Effects of purified eicosapentaenoic and docosahexaenoic acids on glycemic control, blood pressure, and serum lipids in type 2 diabetic patients with treated hypertension. *Am J Clin Nutr.* 2002;76:1007-1015.
31. MacLean C, Mojica W, Morton S, Pencharz J, Hasenfeld Garland R, Tu W, et al. Effects of Omega-3 Fatty Acids on Lipids and Glycemic Control in Type II Diabetes and the Metabolic Syndrome and on Inflammatory Bowel Disease, Rheumatoid Arthritis, Renal Disease, Systemic Lupus Erythematosus, and Osteoporosis. *Evid Rep Technol Assess (Summ).* 2004;(89):1-4
32. Banel D, B Hu F. Effects of walnut consumption on blood lipids and other cardiovascular: a meta-analysis and systematic review1-3 risk factors. *Am J Clin Nutr.* 2009;90:56-63.
33. Jenkins DJ, Hu FB, Tapsell LC, Josse AR, Kendall CW. Possible Benefit of Nuts in Type 2 Diabetes. *J Nutr.* 2008;138(9):1752S-1756S.
34. Curb J, Wergowske G, Dobbs J, Abbott R, Huang B. Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts. *Arch Intern Med.* 2000;160:1154-1158.
35. Lovejoy J, Most M, Lefevre M, Greenway F, Rood J. Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes. *Am J Clin Nutr.* 2002;76(5):1000-1006.
36. Scott L, Balasubramanyam A, Kimball K, Aherns A, Fordis C, Ballantyne C. Long-term, randomized clinical trial of two diets in the metabolic syndrome and type 2 diabetes. *Diabetes Care.* 2003;26:2481-2482.
37. Garg A, Bonanome A, Grundy S, Zhang Z, Unger R. Comparison of a highcarbohydrate diet with a high-monounsaturated- fat diet in patients with noninsulin-dependent diabetes mellitus. *N Engl J Med.* 1988; 319:829-834.
38. Mensink R, Zock P, Kester A, Katan M. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr.* 2003;77:1146-1155.
39. Dolecek T. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial. *Proc Soc Exp Biol Med.* 1992;200:177-182.
40. Hu F, Stampfer M, Manson J, Rimm E, Wolk A, Colditz G, et al. Dietary intake of a-linolenic acid and risk of fatal ischemic heart disease among women. *Am J Clin Nutr.* 1999;69:890-897.
41. Ma Y, Njike VY, Millet J, Dutta S, Doughty K, Treu JA, et al. Effects of Walnut Consumption on Endothelial Function in Type 2 Diabetics: A Randomized, Controlled, Cross-Over Trial. *Diabetes Care.* 2010;33(2):227-232.