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Beneficial effects of ketogenic diet in obese diabetic subjects

Hussein M. Dashti · Thazhumpal C. Mathew · Mousa Khadada · Mahdi Al-Mousawi · Husain Talib · Sami K. Asfar · Abdulla I. Behbahani · Naji S. Al-Zaid

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Abstract

Objective Obesity is closely linked to the incidence of type II diabetes. It is found that effective management of body weight and changes to nutritional habits especially with regard to the carbohydrate content and glycemic index of the diet have beneficial effects in obese subjects with glucose intolerance. Previously we have shown that ketogenic diet is quite effective in reducing body weight. Furthermore, it favorably alters the cardiac risk factors even in hyperlipidemic obese subjects. In this study the effect of ketogenic diet in obese subjects with high blood glucose level is compared to those with normal blood glucose level for a period of 56 weeks.

Materials and methods A total of 64 healthy obese subjects with body mass index (BMI) greater than 30, having high blood glucose level and those subjects with normal blood glucose level were selected in this study. The body weight, body mass index, blood glucose level, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, urea and creatinine were determined before and at 8, 16, 24, 48, and 56 weeks after the administration of the ketogenic diet.

Results The body weight, body mass index, the level of blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and urea showed a significant decrease from week 1 to week 56 ($P < 0.0001$), whereas the level of HDL-cholesterol increased significantly ($P < 0.0001$). Interestingly these changes were more significant in subjects with high blood glucose level as compared to those with normal blood glucose level. The changes in the level of creatinine were not statistically significant.

Conclusion This study shows the beneficial effects of ketogenic diet in obese diabetic subjects following its long-term administration. Furthermore, it demonstrates that in addition to its therapeutic value, low carbohydrate diet is safe to use for a longer period of time in obese diabetic subjects.

Keywords Obesity · Blood glucose · Cholesterol · LDL · HDL · Triglycerides · Low-carbohydrate diet · Ketogenic diet

H. M. Dashti (✉) · S. K. Asfar · A. I. Behbahani
Departments of Surgery, Faculty of Medicine, Kuwait University, PO Box 24923, 13110 Safat, Kuwait
e-mail: info@drdashti.com

T. C. Mathew
Faculty of Medicine and Faculty of Allied Health Sciences, Kuwait University, Safat, Kuwait

M. Khadada
Department of Medicine, Kuwait University, Safat, Kuwait

M. Al-Mousawi · H. Talib
Primary Health Care Salmeiah and Shaab Clinic, Kuwait University, Safat, Kuwait

N. S. Al-Zaid
Department of Physiology, Kuwait University, Safat, Kuwait

Introduction

Obesity is a serious universal health problem [1, 2]. In the United States, two of every three adults are either overweight (BMI of 25–29.9 kg/m^2) or obese (BMI of 30 and above; [3]). Similarly, there is a tremendous increase in the rate of obesity in Kuwait and other Gulf countries. During the last decade there is a high prevalence of obesity in Kuwait [4, 5].

Obesity substantially increases the risk of morbidity from various chronic diseases. There is a tendency for type

II diabetes and obesity to occur together [6–9]. Type II diabetes is characterized by impaired insulin sensitivity (resistance) coupled with the inability of the pancreatic β-cells to produce adequate amount of insulin depending on the increased demand. Obesity is known to aggravate insulin resistance and is an early metabolic defect in nearly all individuals with type II diabetes [10]. Type I diabetes on the other hand is developed by the deficiency of insulin due to destruction of pancreatic β-cells. High blood glucose level leads to complications of vasculopathy, retinopathy, nephropathy, neuropathy, and cardiomyopathy [11, 12].

Although the exact molecular mechanism that link obesity to diabetes needs to be elucidated, one of the causes of metabolic syndrome may be the ectopic accumulation of lipids. Although, adipose tissue is the primary organ of lipid storage, in obese subjects, lipid is deposited into other non-adipose organs, such as liver, skeletal muscle, β-cells, and cardiac tissue. The ectopic lipid deposited in the liver leads to the commonly observed hepatic steatosis or fatty liver. Lipid deposition in skeletal muscle and β -cells leads to insulin resistance, impaired insulin secretion, and eventually type II diabetes [13].

Various studies have shown that reducing weight in obese patients with glucose intolerance, have beneficial effects in delaying or even preventing the progression to diabetes. Thus, effective management of body weight and changes to nutritional habits have beneficial effects in obese diabetic subjects [14, 15]. However, the ideal nature of weight reducing diet program for patients with impaired insulin sensitivity is quite debatable and needs careful monitoring.

Recent studies from our laboratory [16–18] have shown the beneficial effects of ketogenic diet in which the daily consumption of carbohydrate is less than 20 g, regardless of fat, protein, and caloric intake, in overweight and obese patients. We have shown that in addition to reducing the weight in overweight and obese individuals, it reduces the risk factors for cardiovascular diseases even in hyperlipidemic obese subjects [16–18] as compared to other diet programs [19–25].

It is quite logical to assume that excessive intake of carbohydrate may be harmful to individuals with insulin resistance. Following the consumption of a large amount of carbohydrate, there was an obvious increase in the level of blood glucose, insulin, and serum triglycerides in insulin-resistant individuals. In addition, a high carbohydrate diet raises triglyceride levels and reduces HDL-cholesterol along with insulin resistance [26, 27].

Considering the above-mentioned disorders associated with the intake of a high-carbohydrate diet in obese subjects, the purpose of this study was to monitor the changes in body weight, lipid profile, glucose, urea, and creatinine following the administration of a low-carbohydrate, ketogenic diet (LCKD) in overweight and obese diabetic subjects as compared to non-diabetic obese subjects for a period of 56 weeks.

Materials and methods

In this study, 64 healthy obese subjects with body mass index (BMI) greater than 30, having blood glucose level >6.1 mmol/l (Group I; $n = 31$) and those subjects with normal blood glucose level (Group II; $n = 33$) were selected. Subjects with other complex medical histories were not included in this study. The body weight, blood glucose level, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, urea, and creatinine were determined before and at 8, 16, 24, 48, and 56 weeks after the administration of the ketogenic diet. Their average age, body weight, and base line parameters of other biochemical parameters are given in Table 1. All the subjects included in this study were Kuwaitis, with similar dietary habits.

All 64 subjects were instructed to follow a ketogenic diet consisting of less than 20 g of carbohydrates and 80–100 g of proteins in the form of meat, fish, fowl, eggs, shellfish, and

Table 1 Baseline values of different physical and biochemical parameters monitored in persons subjected to low-carbohydrate diet (ketogenic diet)

	Group I (n = 31) High glucose	Group II (n = 33) Normal glucose	P-value
Age (years)	46.4 ± 9.4	40.0 ± 11.4	0.1197
Weight (kg)	108.1 ± 21.2	105.3 ± 15.4	0.5349
Tot. Chol. (mmol/l)	6.8 ± 1.1	5.5 ± 1.3	0.0003
HDL (mmol/l)	1.0 ± 0.3	1.2 ± 0.3	0.0552
LDL (mmol/l)	5.2 ± 0.9	4.0 ± 1.1	0.0002
TG (mmol/l)	4.7 ± 2.5	1.8 ± 1.0	<0.0001
Glucose (mmol/l)	10.5 ± 3.0	5.1 ± 0.4	<0.0001

HDL = high density lipoprotein; LDL = low-density lipoprotein; TG = Triglyceride

Data are expressed as mean ± standard deviation

Table 2 Recommended and restricted food in ketogenic diet

Recommended food			Fully restricted food	
Proteins	Vegetables/Fruits	Oil	Carbohydrates	Fruits/ drinks
Fish: Tuna, Sardine Prawns, Shrimps. Lobster	Spinach, Watercress, Eggplant, Parsley, Mulberry, Coriander, Mint, Artichoke, Okra, Cabbage, Mushroom, Avocado, Leek, Carrot, Radish, Celery, Cauliflower, Green pepper, Lettuce, Cucumber, Tomato, 10–15 olives/ day, Lemon, Strawberry -6/day, Avocado, Berries-10/day	Olive oil (5 tablespoon) added to the salad, Flax seed oil	Flour, Potato, Macaroni Spaghetti, Noodles, Bread, Rice, Sugar, Sweets, Honey, Cakes	All fruit juices, all soft drinks
Meat: Kababs, Sausages, Minced				
Poultry: Chicken, Eggs				
Cheese: Full fat cheese				

cheese. The subjects in this study were not consuming any kind of alcoholic beverages. Polyunsaturated and monounsaturated fats (5 tablespoons olive oil) were included in the diet. A list of recommended and restricted food in ketogenic diet is given in Table 2. Twelve weeks later an additional 20 g of carbohydrates was given. Micronutrients (vitamins and minerals) in the form of 1 capsule/day were given to each subject throughout the study period.

Fasting blood tests were carried out in all the subjects. The subjects were subjected to liver and renal function tests, complete blood count, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL; directly measured), triglycerides (TG), urea and creatinine in the beginning after 8, 16, 24, 32, 40, 48 and 56 weeks. Biochemical analysis of lipid, liver, renal profiles and electrolytes were performed by Beckman CX 5 C E and complete blood count was carried out by Coulter MD II. The body mass index (the weight in kilograms divided by square of the height) was determined initially and after 8, 16, 24, 32, 40, 48 and 56 weeks. We standardized our results with daily internal and external quality control program with ''Lab quality Finland.'' During each visit, enquiries were made regarding their adherence to the diet, exercise habits and any side effects or uncomfortable feelings they felt.

Most of the subjects as advised by their General Practitioners were following at least a daily walk of 45 min before participating in this program and we allowed them to continue with their routines.

Statistical differences between different parameters before and after the administration of ketogenic diet were analyzed by student-*t* test using a computer software package (Stat view 4.02). Age, weight and all biochemical parameters were expressed as mean ± standard deviation.

Results

Statistical significance between week 1 and week 56 observation of various parameters studied in total, group I (high blood glucose level) and group II (normal blood glucose level) subjects is given in Table 3. There was a significant reduction in the body weight (Fig. 1) in Group I (high blood glucose) and Group II (normal blood glucose) throughout the program. The effect of gender in body weight was not significant. The level of total cholesterol decreased significantly after week 1 until the end of the study (Fig. 2). HDL-cholesterol increased significantly (Fig. 3), whereas LDL-cholesterol decreased significantly (Fig. 4). The level of triglycerides significantly decreased from the start till the end of the study (Fig. 5). The blood glucose level of both the groups decreased significantly from the start until the 56th week (Fig. 6). HDL/LDL ratio (Fig. 7) showed a significant increase in both the groups ($P < 0.0001$). The data in Figs. 1–7 are expressed as mean ± standard error. Percentage changes at the end of the study (56 weeks) in the various parameters observed are given in Table 4. There was a significant decrease in urea at week 1 and week 56 (Table 3). The changes in the level of creatinine were not statistically significant.

Discussion

Ketosis is a natural phenomenon that occurs in man during fasting and lactation. Administration of this diet mimics the effects of starvation. Ketogenic diet has been around in the medical literature for well over 70 years [16, 17], especially as an effective treatment for controlling seizures. In some instances it is actually better than the modern

Table 3 Statistical significance between week 1 and week 56 observation of various parameters studied in total, group I (high glucose level) and group II (normal glucose level) subjects

	Group I (*n* = 31; High Glucose)			Group II (*n* = 33; Normal Glucose)		
	Week 1	Week 56	*P*-Value	Week 1	Week 56	*P*-Value
Weight (kg)	108.081 ± 21.245	83.536 ± 18.030	<0.0001	105.273 ± 15.377	74.923 ± 11.384	<0.0001
Tot. Chol. (mmol/l)	6.755 ± 1.086	4.878 ± 0.533	<0.0001	5.479 ± 1.293	4.650 ± 0.495	0.0020
HDL (mmol/l)	1.033 ± 0.264	1.586 ± 0.211	<0.0001	1.237 ± 0.270	1.621 ± 0.177	<0.0001
LDL (mmol/l)	5.160 ± 0.892	3.379 ± 0.608	<0.0001	4.030 ± 1.148	2.807 ± 0.496	<0.0001
TG (mmol/l)	4.681 ± 2.468	1.006 ± 0.205	<0.0001	1.827 ± 0.981	0.861 ± 0.179	0.0001
Glucose (mmol/l)	10.481 ± 3.026	4.874 ± 0.556	<0.0001	5.127 ± 0.440	4.726 ± 0.529	0.0069
Urea (μmol/l)	5.778 ± 0.905	4.972 ± 1.050	0.0111	5.563 ± 1.299	4.419 ± 0.743	<0.0001

HDL = high density lipoprotein; LDL = low-density lipoprotein; TG = Triglyceride BMI = body mass index

Data are expressed as mean ± standard deviation

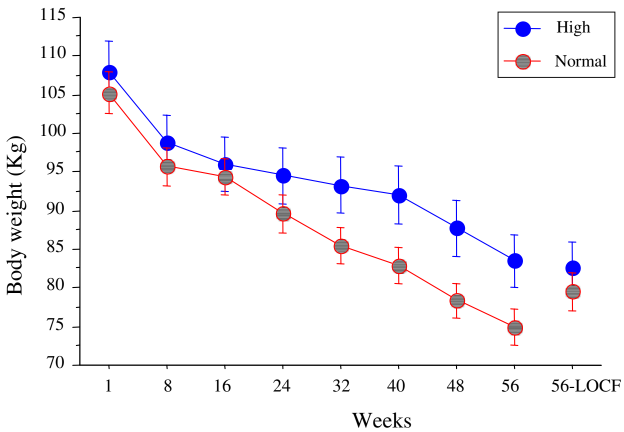

Fig. 1 Changes in body weight after the administration of ketogenic diet for 56 weeks

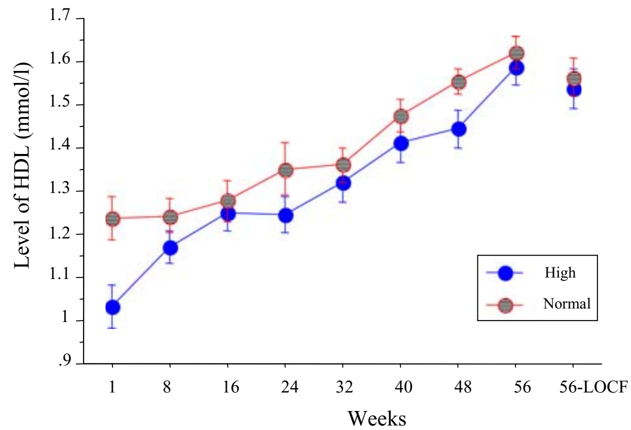

Fig. 3 Changes in the level of HDL after the administration of ketogenic diet for 56 weeks. (HDL = high density lipoprotein)

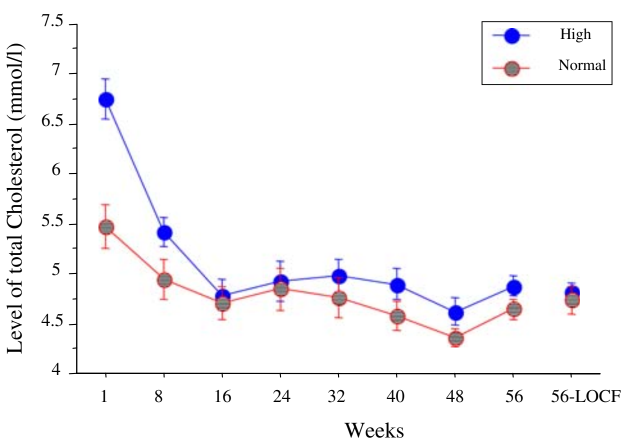

Fig. 2 Changes in the level of total cholesterol after the administration of ketogenic diet for 56 weeks

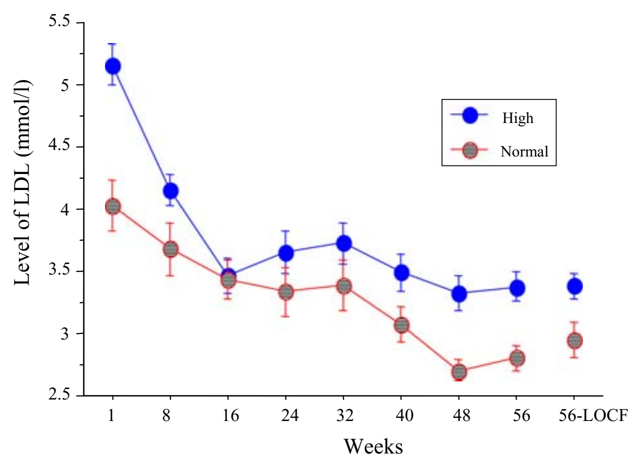

Fig. 4 Changes in the level of LDL after the administration of ketogenic diet for 56 weeks (LDL = low-density lipoprotein)

anti-convulsants at controlling seizures. In a recent study [28], ketone bodies have been used as therapeutic agents for the treatment of: (a) diseases of substrate insufficiency or insulin resistance, (b) diseases resulting from free radical damage, and (c) disease resulting from hypoxia. These studies on ketone body metabolism suggest that mild

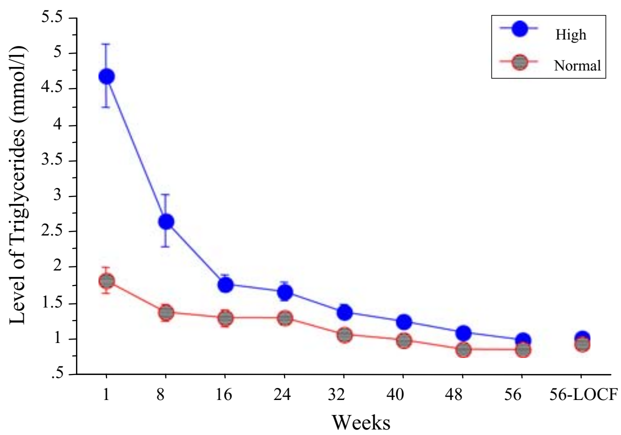

Fig. 5 Changes in the level of tryglycerides after the administration of ketogenic diet for 56 weeks (TG = Triglyceride)

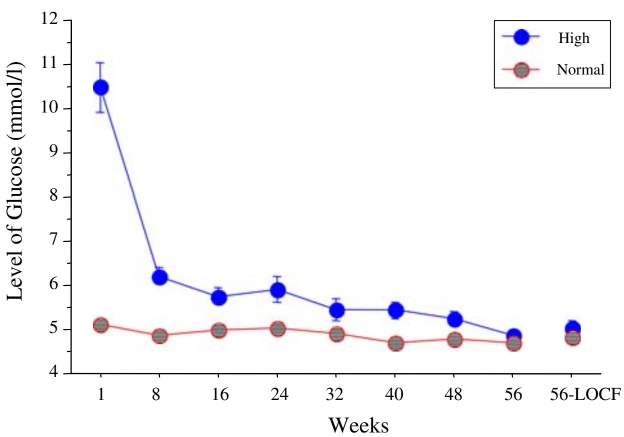

Fig. 6 Changes in the level of blood glucose after the administration of ketogenic diet for 56 weeks

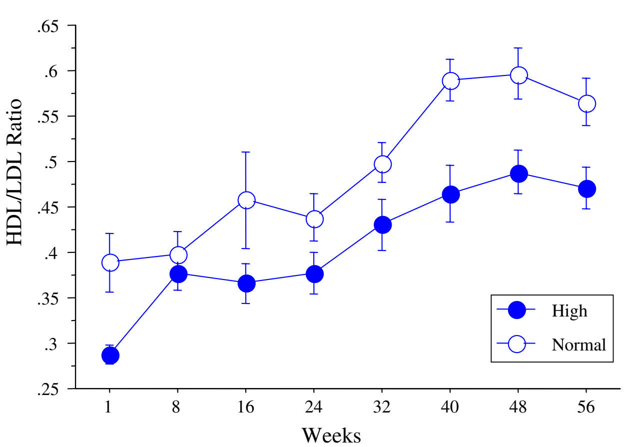

Fig. 7 Changes in HDL/LDL Ratio after the administration of ketogenic diet for 56 weeks (HDL = high density lipoprotein; LDL = low-density lipoprotein)

ketosis may offer therapeutic potential in a variety of different common and rare disease states.

There is an urgent need for identifying effective therapies for obesity, as obesity and obesity associated metabolic disorders have become a serious burden on the health care systems of various countries. Substantial evidence from various studies indicates that very-low-carbohydrate diets are effective for weight loss. As mentioned above, ketogenic diet has been around in the medical literature for well over 70 years [16, 17]. However, several research teams are revisiting very-low-carbohydrate diets to confirm the beneficial claims of ketogenic diet using the current research methodologies and techniques.

This study shows the beneficial effects of ketogenic diet following its long-term administration in obese diabetic and non-diabetic subjects. It significantly reduces the body weight and body mass index. The level of total cholesterol decreased significantly after week 1 until the end of the study. As per the Friedewald formula for LDL cholesterol: LDL-cholesterol = Total cholesterol–(triglycerides/5)–HDL-cholesterol. Thus, Total cholesterol = LDL-cholesterol + HDL-cholesterol + (triglycerides/5) Furthermore, it decreases the level of triglycerides, and LDL-cholesterol. The level of HDL-cholesterol increased significantly in both the groups. The level of triglycerides significantly reduced after. Glucose level decreased significantly. The level of urea showed significant decrease in both the groups. No significant alteration was noticed in renal function test. In this study the HDL/LDL ratio showed a significant increase in both the groups. The LDL/HDL or HDL/LDL ratio is actually a more pure ratio than total cholesterol/HDL. Since LDL is a measure of bad cholesterol and HDL is a measure of good cholesterol, whereas the total cholesterol is the sum of HDL, LDL, and the VLDL.

Most of the studies that dealt with the effect of different diet on obesity [29–33] have clearly shown that people lost more weight on very-low-carbohydrate diets than on diets that contained the same number of calories but more carbohydrates. The only study, to our knowledge that did not demonstrate greater weight loss with the very-low-carbohydrate diet, the energy content of the diet was low (600 kcal/day) and the subjects were >45 kg of body weight [34].

As mentioned in the materials and methods section, most of the subjects were following at least a daily walk of 45 min before participating in this program. However, they have not experienced any reduction in the body weight. In this study, we just allowed them to continue with their routine exercise habits. Thus, we have not introduced a new pattern of exercise together with this diet and obviously, the observed beneficial effects were not related to exercise.

In this study, polyunsaturated and monounsaturated fats (5 tablespoons olive oil) were included in the diet. Olive oil is one of the most characteristic components of

Table 4 Percentage changes in the various parameters after the administration of ketogenic diet for 56 weeks

Change at week 56 (%)	Total (n = 64)	Group I (n = 31) High glucose	Group II (n = 33) Normal glucose	P-value
Weight (kg)	–25.8 ± 6.4	–24.4 ± 6.7	–27.2 ± 6.0	0.3167
Tot. Chol. (mmol/l)	–19.3 ± 17.0	–28.5 ± 11.1	–9.0 ± 16.7	0.0096
HDL (mmol/l)	52.3 ± 43.8	63.4 ± 51.1	39.8 ± 30.0	0.9522
LDL (mmol/l)	–28.2 ± 20.1	–33.0 ± 20.4	–22.9 ± 18.7	0.5467
TG (mmol/l)	–59.0 ± 32.0	–40.8 ± 38.0	–40.8 ± 38.0	0.0039
Glucose (mmol/l)	–31.0 ± 25.0	–50.9 ± 12.5	–7.4 ± 11.9	<0.0001

HDL = high density lipoprotein; LDL = low-density lipoprotein; TG = Triglyceride BMI = body mass index

Data are expressed as mean ± standard deviation. Statistical significance between Group I and Group II are given

Mediterranean diet [35]. It has a protective role in cardiovascular diseases, and various cancers, as well as to diminish the age-related cognitive decline [35–37]. Olive oil is rich in monounsaturated fatty acids and antioxidant substances. The health benefits of olive oil are attributed to these factors. Furthermore, it is shown that olive oil may have protective role for the dynamic blood cholesterol levels in a healthy population [37]. Although olive oil has several beneficial effects, it should be noted that in our previous study [16], we have not included olive oil in the diet and the decrease in weight in obese subjects was similar in both the studies.

A meta-analysis compared the effects of low-carbohydrate diets (maximum carbohydrate intake 60 g daily) with those of low-fat, energy-restricted diets on weight loss [38, 39]. In this meta-analysis, five randomized controlled trials were analyzed, with 6–12 months' duration. It is found that after 6 months, the subjects on a low-carbohydrate diet had lost more weight than those on a low-fat diet. We have noticed a severe weight loss during the initial period as compared to other time points. The overall decrease in weight during the study period (56 weeks) was quite significant. It should be noted that in this study only 20 grams of carbohydrate is given initially and after 12 weeks an additional 20 grams is added to the diet. On the other hand in the above studies [38, 39] the carbohydrate intake was about 60 grams daily. In addition, genetic nature of the population may have influenced these variations.

This study also compared the effect of a low-carbohydrate diet and low-fat diet on the risk factors for cardiovascular disease. It is found that after 6 months, more favorable changes in the level of triglyceride and HDL-cholesterol were observed in the low-carbohydrate group. However, total cholesterol and LDL-cholesterol level changes were more favorable in the low-fat group. In our study, total cholesterol, LDL-cholesterol and triglycerides showed a significant decrease from week 1 to week 56 ($P < 0.0001$), whereas the level of HDL-cholesterol increased significantly ($P < 0.0001$). This again may be due to the difference in carbohydrate intake and the general food habits of the population studied. Furthermore, as mentioned above genetic factors may affect the lipid profile. However, further studies are required to understand the exact mechanisms of the results observed in this study.

Several possible mechanisms on the role of very-low-carbohydrate have been suggested. It is thought that major part of the weight loss following the administration of ketogenic diet could be due to the loss of water. It is also shown that very-low-carbohydrate ketogenic diets may alter the metabolic rate by preserving more lean body mass [40]. There is a greater loss of energy in the form of heat [41] and in the form of ketones in urine, sweat, and feces.

Studies that have assessed body composition on a very-low-carbohydrate ketogenic diet have shown that there is a preferential loss of fat mass and preservation of lean body mass following the administration of ketogenic diet [40, 42, 43]. Prolonged administration of very-low carbohydrate diets did not cause any chronic dehydration [44]. It is generally thought that very-low-carbohydrate diets, especially if high in saturated fat, might lead to insulin resistance. However, contrary to this belief recent studies indicate that very-low carbohydrate diets do not have an adverse effect on glucose metabolism or insulin resistance [45–47].

In conclusion, the data presented in this study shows the beneficial effects of ketogenic diet in obese diabetic subjects following its long-term administration. Furthermore, low-carbohydrate, ketogenic diet (LCKD) may be effective for improving glycemia and reducing medications in patients with type II diabetes.

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References

1. Bray GA (1976) The risks and disadvantages of obesity. The obese patient. Saunders, Philadelphia, pp 215–251

2. Pi-Sunyer FX (1993) Medical hazards of obesity. Ann Intern Med 119: 655–660
3. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM (2006) Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 295:1549–1555
4. Al-Isa AN (2003) Are Kuwaitis getting fatter?. Nutr Health 17(3): 185–197
5. Al-Isa AN, Thalib L (2006) Body mass index of Kuwaiti children aged 3–9 years: reference percentiles and curves. J R Soc Health 126(1):41–46
6. National Diabetes Commission (1976) Report of the National Diabetes Commission on Diabetes to the Congress of the United States. Washington, DC, U.S. Govt. Printing Office, (DHEW publ. no. 1:1019)
7. Colditz GA (1995) The Nurses' Health Study: a cohort of US women followed since 1976. J Am Med Women's Assoc 50:40–44
8. Harder H, Dinesen B, Astrup A (2004) The effect of a rapid weight loss on lipid profile and glycemic control in obese type 2 diabetic subjects. Int J Obes Relat Metab Disord 28(1): 180–182
9. Hossain P, Kawar B, Nahas M-El (2007) Obesity and Diabetes in the Developing World -A Growing Challenge. N Engl J Med 356(3): 213–215
10. Ford ES, Giles W (2003) A comparison of the prevalence of the metabolic syndrome using two proposed definitions. Diabetes Care 26:575–581
11. Kissebah AH, Freedman DS, Peiris AN (1989) Health risks of obesity. Med Clin North Am; 73:111–138
12. Bray GA (2004) Medical consequences of obesity. J Clin Endocrinol Metab; 89:2583–2589
13. Molavi B, Rasouli N, Kern PA (2006) The prevention and treatment of metabolic syndrome and high-risk obesity Curr Opin Cardiol 21:479–485
14. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM (2002) The Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346:393–403
15. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laasko M, Louheranta A, Rastas M, Salminen V, Uusitupa M (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 344:1343–1350
16. Dashti HM, Bo-Abbas YY, Mathew TC, Hussein T, Behbehani A, Khoursheed M, Al-Sayer HM, Al-Zaid NS (2003) Ketogenic Diet Modifies the Risk Factors for Heart Disease in Obese Patients. Nutrition 19: 901–902
17. Dashti HM, Mathew TC, Hussein T, Asfar SK, Behbehani AI, Al-Sayer HM, Al-Zaid NS. (2004) Long term effects of ketogenic diet in obese subjects. Exp Clin Cardiol 9(3): 200–205
18. Dashti HM, Al-Zaid NS, Mathew TC, Al- Mouzawi M, Talib H, Asfar SK, Behbehani AI. (2006) Long term effects of ketogenic diet in obese subjects with high cholesterol level. Mol Cellular Biochem 286: 1–9
19. Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC (2004) A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. Ann Intern Med 140(10):769–777
20. Westman EC, Mavropoulos J, Yancy WS, Volek JS (2003) A review of low carbohydrate ketogenic diets. Curr Atheroscler Rep 5(6):476–483
21. Kwiterovich PO Jr, Vining EP, Pyzik P, Skolasky R Jr, Freeman JM (2003) Effect of a high-fat ketogenic diet on plasma levels of lipids, lipoproteins, and apolipoproteins in children. JAMA 290(7):912–920
22. Sharman MJ, Kraemer WJ, Love DM, Avery NG, Gomez AL, Scheett TP, Volek JS (2002) A ketogenic diet favorably affects serum biomarkers for cardiovascular disease in normal-weight men. J Nutr 132(7):1879–1885
23. Lofgren IE, Herron KL, West KL, Zern TL, Patalay M, Koo SI, Fernandez ML (2005) Carbohydrate intake is correlated with biomarkers for coronary heart disease in a population of overweight premenopausal women. J Nutr Biochem 16(4):245–250
24. Boden G, Sargrad K, Homko C, Mozzoli M, Stein TP (2005) Effect of a low-carbohydrate diet on appetite, blood glucose levels, and insulin resistance in obese patients with type 2 diabetes. Ann Intern Med 142(6):403–411
25. Ezenwaka CE, Kalloo R (2005) Carbohydrate-induced hypertriglyceridaemia among West Indian diabetic and non-diabetic subjects after ingestion of three local carbohydrate foods. Indian J Med Res 121(1): 23–31
26. Taubes G (2001) Nutrition: the soft science of dietary fat. Science 291:2536–2545
27. Zammit VA, Waterman IJ, Topping D, McKay G (2001) Insulin stimulation of hepatic triacylglycerol secretion and the etiology of insulin resistance. J Nutr 131:2074–2077
28. Veech RL (2004) The therapeutic implications of ketone bodies: the effects of ketone bodies in pathological conditions: ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. Prostaglandins Leukotrienes and Essential Fatty Acids 70:309–319
29. Rabast U, Vornberger KH, Ehl M (1981) Loss of weight, sodium and water in obese persons consuming a high- or lowcarbohydrate diet. Ann Nutr Metab 25:341–349
30. Rabast U, Schonborn J, Kasper H (1979) Dietetic treatment of obesity with low and high-carbohydrate diets: comparative studies and clinical results. Int J Obes 3:201–211
31. Rabast U, Kasper H, Schonborn J (1978) Comparative studies in obese subjects fed carbohydrate-restricted and high carbohydrate 1,000-calorie formula diets. Nutr Metab 22:269–277
32. Yang MU, Van Italie TB (1976) Composition of weight lost during short-term weight reduction. J Clin Invest 58:722–730
33. Young CM, Scanlan SS, Im HS, Lutwak L (1971) Effect on body composition and other parameters in obese young men of carbohydrate level of reduction diet. Am J Clin Nutr 24:290–296
34. Vazquez JA, Adibi SA (1992) Protein sparing during treatment of obesity: ketogenic versus nonketogenic very low calorie diet. Metabolism 41:406–414
35. Battino M, Ferreiro MS (2004) Ageing and the Mediterranean diet: a review of the role of dietary fats. Public Health Nutr 7(7):953–958
36. La Vecchia C (2004) Mediterranean diet and cancer. Public Health Nutr (7):965–968
37. Shahtahmasebi S, Shahtahmasebi S (2004) A case follow-up report: possible health benefits of extra virgin olive oil. Scientific World J 4:853–858
38. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS Jr, Brehm BJ, Bucher HC (2006) Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med 166: 285–293
39. Malik VS, Hu FB. (2007) Popular weight-loss diets: from evidence to practice. Nat Clin Pract Cardiovasc Med 4(1):34–41
40. Volek JS, Sharman MJ, Love DM, Avery NG, Gomez AL, Scheett TP, Kraemer WJ (2002) Body composition and hormonal responses to a carbohydrate-restricted diet. Metabolism 51:864–870
41. Kasper H, Thiel H, Ehl M (1973) Response of body weight to a low carbohydrate, high fat diet in normal and obese subjects. Am J Clin Nutr 26:197–204

42. Benoit FL, Martin RL, Watten RH (1965) Changes in body composition during weight reduction in obesity. Ann Intern Med 63:604–612
43. Willi SM, Oexmann MJ, Wright NM, Collop NA, Lyndon L (1998) The effects of a high-protein, low-fat, ketogenic diet on adolescents with morbid obesity: body composition, blood chemistries, and sleep abnormalities. Pediatrics 101:61–67
44. Volek JS, Gómez AL, Kraemer WJ (2000) Fasting and postprandial lipoprotein responses to a low-carbohydrate diet supplemented with n-3 fatty acids. J Am Coll Nutr 19:383–391
45. Cutler DL, Gray CG, Park SW, Hickman MG, Bell JM, Kolterman OG (1995) Low-carbohydrate diet alters intracellular glucose metabolism but not overall glucose disposal in exercise-trained subjects. Metabolism 44:1264–1270
46. Bisschop PH, de Metz J, Ackermans MT, Endert E, Pijl H, Kuipers F, Meijer AJ, Sauerwein HP, Romijn JA (2001) Dietary fat content alters insulin-mediated glucose metabolism in healthy men. Am J Clin Nutr 73:554–559
47. Bisschop PH, Pereira Arias AM, Ackermans MT, Endert E, Pijl H, Kuipers F, Meijer AJ, Sauerwein HP, Romijn JA (2000) The effects of carbohydrate variation in isocaloric diets on glycogenolysis and gluconeogenesis in healthy men. J Clin Endocrinol Metab 85:1963–1967