Impact of low carbohydrate diet on patients with type 1 Diabetes

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Abstract: Introduction: Achieving glycemic control in subjects with type 1 diabetes presents a significant challenge to the patient and the healthcare providers. The recommendations for dietary carbohydrates varied over the years from severe restriction to no restriction. We aim to study the impact of low carbohydrate diet on subjects with type 1 diabetes.
Subjects and Methods: we conducted a cross over clinical trial in which 46 uncontrolled (HbA1c ≥7%), subjects with type 1 diabetes on a standard carbohydrate diet, were placed on low carbohydrate diet (<26% of daily caloric intake). Patients attending Ain Shams University hospitals outpatient diabetes clinics were invited to participate. Participants were provided with education sessions to achieve and maintain low carbohydrate diet. They visited the clinic at baseline, 3 and 6 months.
Results: low carbohydrate diet resulted in significant improvement ($p<0.001$) in the following parameters using repeated measure analysis of variance: HbA1c (9.2 to 6.6%), weight (82.7kg to 76.7kg), BMI (29.70 to 27.56 Kg/m^2), percent body fat (36.7 to 30.2%), skeletal muscle mass (53.8 to 55.9kg), total daily dose of insulin (72 to 54 IU) total cholesterol (199 to 169 mg/dL), LDL (119 to 101mg/dL) triglycerides (182 to 113 mg/dL), ALT (23 to 20IU/L), AST (14 to 12 IU/L), UAC ratio (15.7 to 14.0mg/g) and decreased incidence of hypoglycemic and hyperglycemic events (4.4 to 1.1 and 20.8 to 4.0 events/week respectively).
Conclusion: low carbohydrate diet demonstrated efficacy in terms of glycemic control and attainment of glycemic targets with good safety profile in terms of lower rates of hypoglycemic events.

Keywords: type 1 diabetes, low carbohydrate diet, body composition, glycemic control, skeletal muscle mass

1. Introduction

Extremely low carbohydrate diets were once the only available treatment for type 1 diabetes. The discovery of insulin a century ago was a revolution in the management of this chronic autoimmune disorder. With development of advanced flexible insulin regimens, recommendations shifted to almost usual eating patterns with matching of doses to carbohydrate content. (1) In the 1960s, concerns were raised about the risks of a low

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carbohydrate, high saturated fat diet in an atherogenically at-risk population and recommendations shifted to decrease fat intake (<35% of energy) and increase carbohydrate intake to around 50-55% of total energy intake. The advice was that most of the carbohydrates to be ingested are complex in nature. For several years now, low fat and high carbohydrate diets have been advocated as healthy eating for people with and without diabetes. (2). However, an analysis of the food consumption pattern during the more recent “obesity epidemic” found that the increase in calories was almost entirely due to an increase in carbohydrates (3,4) Today, the prevalence of obesity in subjects with type 1 diabetes is at alarming levels. (5). Despite the availability of advanced insulins, affected individuals remain at high risk of serious complications due to the chronic hyperglycaemia (6). New interventions include decreasing carbohydrate intake to decrease attacks of elevated blood glucose by limiting the carbohydrate intake.

Insulin doses will also decrease following the reduced carbohydrate intake, reducing the risk of hypoglycaemia. (5) There is emerging evidence that low carbohydrate intake (defined as <26% of daily dietary intake or below 130grams per day (7) may be a relevant strategy for many people if weight loss and the prevention of both hypo- and hyperglycaemia is a concern (5). The standard carbohydrate diet is carbohydrate: protein: fat 45-65%:10-35%:20-35%. (2). We aim to study the impact of “Low carbohydrate” diet on patients with type 1 diabetes.

2. Materials and Methods

Study design,_Our study was a cross-over clinical trial, performed in the outpatient Diabetes Clinics of Ain-Shams University Hospital, Cairo, Egypt from October 2019 till June 2021. The primary outcome for this study was glycemic control as indicated by HbA1c measurement.

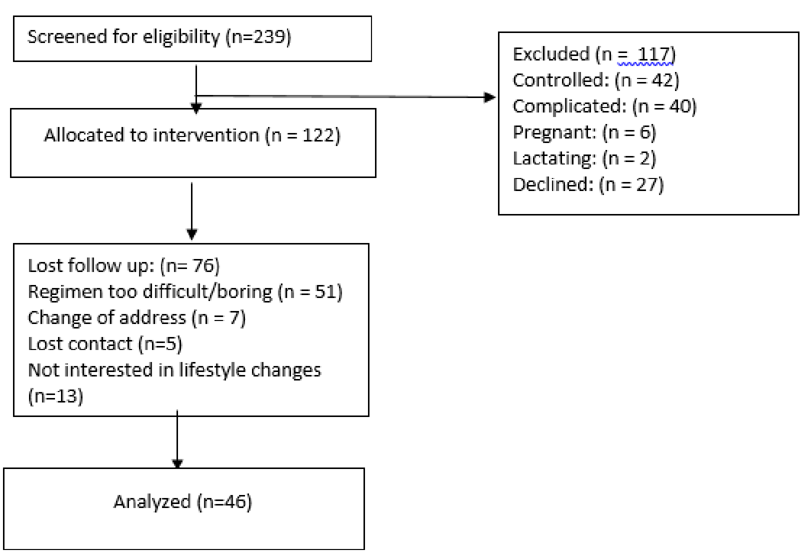

Figure1: Enrolment, allocation, and attrition of participants

The improvement in HbA1c at 3 and 6 months was used to estimate the sample size of at least 34 data pairs to achieve 80% power to detect significant effect of the intervention.

Secondary outcome parameters included: hyper- and hypoglycemic episodes and total daily insulin dose. Anthropometric parameters: weight, BMI, percent body fat and skeletal muscle mass. Laboratory parameters: lipid profile, ALT, AST, creatinine, serum albumin, CBC and urinary albumin/creatinine ratio. All parameters were assessed at baseline, 3 and 6 months.

Subjects were included if they were Egyptian individuals with type 1 diabetes, 18 years of age or more, already performing carbohydrate counting and adequate self-monitoring of blood glucose with appropriate medical visits for at least 6 months and still having an HbA1c ≥7%.

Subjects were excluded if they were pregnant or breastfeeding or had any diabetes complications. All those meeting the inclusion criteria were approached to participate in our study. Those who were willing to join the study signed an informed written consent and underwent baseline clinical and laboratory assessment. 239 patients with type 1 diabetes were screened for eligibility. Enrolment, allocation, and attrition of the participants are shown in Figure 1.

Intervention, We performed a nutritional intervention in patients with type 1 diabetes. Candidates were shifted from standard carbohydrate diet to a low carbohydrate diet which included less than 130 grams of carbohydrates of an average 2000 calorie diet or below 26% of daily caloric requirements.

The subjects were given the dietary program schedule. This included a baseline introductory visit, then consecutive weekly visits for 3 weeks, followed by two visits at 3 months and at 6 months. In between visits the patients were allowed telephone conferences if needed.

The first session was 2-3 hours. During the first hour, low carbohydrate diet was explained using real photo examples for the different meals and snacks and foods rich in unsaturated foods advised. Then each patient was tutored separately to tailor the regimen to suit the socioeconomic status, food preferences, meal timings and to modify the insulin doses. Common low carbohydrate choices (photos) were printed on sticker paper and labeled with the weight in grams (or spoons), calories and carbohydrate content. Caloric requirements were set using the Dietary guidelines of the Americans (8) and then the calories divided as follows: carbohydrates <26%, protein 24-30%, fat 44-50%. The nutritional details for each food item were devised from Carbs and Cals books as World Foods (9) and Carb and Calorie counter (10) and then translated to Arabic. At the end of the first visit, they were given handouts that included their meal plans, carbohydrate exchange lists and self-monitoring tables.

The consecutive 3 visits (weekly visits) were 2 hours long. The first hour was a group meeting where common concerns were clarified, and new low carbohydrate recipes shared. The following hour was again a doctor to patient meeting where any complaints were dealt with, and the self-monitoring diaries seen to modify doses and to ensure compliance. When the COVID 19 pandemic started, there were tight regulations including reducing the number of patients visiting the clinic and the number allowed to be in one room at a single moment with a doctor. The visits were rescheduled to suit the regulations and for many of the visits we required video calling software like Zoom, Botim or Whatsapp to conduct the follow up.

Outcome measures, HbA1c as a surrogate for glycemic control, was measured in a venous blood sample using quantitative colorimetric determination of glycated hemoglobin (HbA_1C) (Trivelli, 1971) Procedure No. 0350 from Stanbio-Laboratory, Inc., USA in our hospital laboratory.

Anthropometric measures taken were weight (Kg), height (cm) and body composition assessment using InBody 120 body composition scale from which we generated results for BMI (Kg/m^2), percent body fat (%) and skeletal muscle mass (Kg). The venous blood

sample was also used to analyse the following using standard commercial assays: lipid profile, ALT, AST, creatinine, serum albumin (Beckman Coulter Life Sciences, Inc.). CBC was done using a blood cell counter. Albumin/creatinine ratio in urine was measured using ACR Assay Kit from Biovision.
Total daily insulin doses were recorded in the handouts. These results were then fed into an Excel sheet to calculate the average total daily dose.
Incidence of hypoglycaemic events (defined as blood sugar below 70mg/dL) and hyperglycaemic events (defined as blood sugar above 180_mg/dL) (11) per week were extracted from the handouts and an average per week calculated.

Statistical methods, The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. The following statistics were used. (i)Descriptive statistics: 1. Mean, Standard deviation (± SD) and range for parametric numerical data, 2.Frequency and percentage of non-numerical data. (ii)Analytical statistics: 1._Repeated Measure Analysis of Variance (RMANOVA test) was used to assess the statistical significance of the difference between more than two study group means. 2. Post Hoc Test was used for comparisons of all possible pairs of group means. P- value: level of significance_-P>0.05: Non significant (NS), P< 0.05: Significant (S).

Ethical considerations,The Research Ethics Committee at Faculty of Medicine, Ain Shams University viewed the protocol and approved its implementation. (Approval Number FMASU MD 287/2019)

3. RESULTS

46 participants, 29 women (64.4%) and 17 men (35.5%), aged 29.80 ± 9.24 years with a range from 19-54 years, completed the study. Mean duration of diabetes was 16.20 ± 8.69 years with a range from 4 to 38 years.

HbA1c

Table 1 shows the HbA1c on enrollment was 9.2 ±1.3%. After 3 months of low carbohydrate diet 21 candidates (45.6%) achieved target HbA1c (7.1±0.8%) and by the end of the study 36 candidates (78.3%) had achieved it with a mean HbA1c 6.6 ±0.6%. The cases achieved a significant mean reduction of 2.1% (p= 0.000) in the first 3 months and a 2.6% (p<0.001) in a total of 6 months of low carbohydrate diet. However, 10 candidates (21.7%) did not achieve target HbA1c after 6 months of low carbohydrate diet.

Secondary outcomes,Table 1 shows a significant reduction (p<0.001) in total daily insulin dose from 72 to 54 IU/day, a mean decline of 15 IU/ day. This represents a 24.6% reduction from baseline total daily insulin dose. The incidence of hypoglycaemic and hyperglycaemic events improved significantly (p<0.001). The mean of hypoglycaemic events declined from a mean of 4 events/week at baseline to 1 event/week (-75%) after 6 months of low carbohydrate diet. The mean of hyperglycaemic events declined from a mean of 20 events/week to 4 events/week (-80%) at 6 months.

There was a significant reduction in mean weight, 4.3kg (p=0.000) and 6.0kg (p<0.001) in the first 3 months and at end of the 6 months respectively. This represents of total of 7.2% reduction in 6 months. This reflected in a significantly lower BMI and percent body fat. The subjects showed a lower BMI by 1.5Kg/m^2 in the first 3 months and 2.1Kg/m^2 in 6 months. There was significant reduction (p<0.001) in the mean BMI from 29.7 Kg/m^2 to 27.6 Kg/m^2 in 6 months which is a 7.1% reduction. The percent body fat showed a significant (p<0.001) 4.9% reduction in the first 3 months. There was a 6.6% reduction in 6 months which is a total of 17.9% reduction from baseline. There was a non-significant gain of skeletal muscle mass (0.4Kg) (p=0.339) in the first 3 months. It became significant (2.1Kg) ($p<0.001$) at the end of the 6 months with a 3.9% increase in comparison to baseline. The results also showed a significant improvement ($p<0.001$) of total cholesterol, triglycerides and LDL on following low carbohydrate diet for 6 months. The reduction from baseline results was 30 (-15.1%), 69(-38.3%), 18 (-15.1%) mg/dL respectively. There was a non-significant change in HDL. A significant reduction in mean ALT, AST, albumin and urinary albumin/creatinine ratio was also observed with the fact that all values remained within the normal reference range. No changes were noted in the haemoglobin or creatinine levels.

Table1: The mean of each parameter at baseline and at 3 and 6 months

Variable	Results at baseline	Results at 3 months	P (1)	Results at 6 months	P(2)	Change%*
HbA1c (%)	9.2±1.3	7.1±0.8	0.000	6.6 ±0.6	<0.001	-28.3
Total daily dose of insulin (IU)	72.3± 23.5	56.7± 16.4	0.000	54.2± 13.7	<0.001	-24.6
Incidence of hypoglycaemic events per week	4.4 ± 2.0	1.3± 0.9	0.000	1.1 ± 0.7	<0.001	-75.0
Incidence of hyperglycaemic events per week	20.9± 8.1	5.7 ± 3.7	0.000	4.1± 2.7	<0.001	-80.3
Weight (Kg)	82.7 ± 17.5	78.4± 14.2	0.000	76.7 ± 13.0	<0.001	-7.2
BMI (Kg/m^2)	29.7 ± 5.9	28.2± 4.8	0.000	27.6± 4.3	<0.001	-7.1
Percent body fat (%)	36.8± 9.9	31.9 ± 8.4	0.000	30.2 ± 8.1	<0.001	-17.9
Skeletal muscle mass (Kg)	53.8 ± 11.1	54.2 ± 11.6	0.339	55.9 ± 12.8	<0.001	3.9
Total cholesterol (mg/dL)	199 ± 49	176±33	0.000	169 ± 27	<0.001	-15.1
Triglycerides (mg/dL)	182± 82	121± 33	0.000	113 ± 28	<0.001	-38.3
LDL (mg/dL)	119 ± 39	108 ± 30	0.017	101± 25	<0.001	-15.1
HDL (mg/dL)	44± 7	46 ± 7		46± 6	0.052	
ALT (IU/L)	23± 6	20± 5	0.000	20± 5	<0.001	-13.0
AST(IU/L)	14± 5	13± 4	0.040	12 ± 4	0.002	-14.3
Urinary albumin/creatinine ratio (mg/g)	16± 6	14± 5	0.001	14± 5	<0.001	-12.5
Albumin (g/dL)	4.0± 0.2	4.0± 0.2	0.022	4.0± 0.2	0.008	
Haemoglobin (grams)	13.5 ± 1.3	13.5 ± 1.2		13.5± 1.3	0.994	
Creatinine (mg/dL)	0.8± 0.2	0.8± 0.1		0.8± 0.1	0.927	

The results are shown in mean±standard deviation. P(1) is the p-value for the difference between the start and 3 months calculated by post hoc test. P(2) is the p value calculated by repeated measure ANOVA test for the difference between baseline and 6 months. * the percentage change between baseline and 6 months. All means were rounded to the nearest whole number or nearest tenth according to the usual reference range results.

4. Discussion

Our study revealed a significant reduction in the HbA1c level following low carbohydrate diet for 3 months which was maintained at 6 months. By the end of 6 months more than 70% of our study subjects achieved their target HbA1c. The Diabetes Complications and Control Trial (DCCT) established glycosylated hemoglobin (A1C) as the gold standard of glycemic control. Levels < 7% are considered appropriate for reducing the risk of vascular complications. (12) For this reason our primary outcome was HbA1c reduction to the recommended range. Krebs et al, studied the effect of a low carbohydrate diet (75grams per day) on 10 subjects with type 1 diabetes and found a significant reduction in HbA1c after 3 months (1). Similarly, Nielsen et al, studied the same dietary regimen on 48 attendees and found a significant HbA1c reduction.(13) O'Neill et al reviewed 30 patients on a low carbohydrate regimen and found similar reduction in HbA1c (14).

There was a significant reduction of total daily insulin dose (15 units) at 3 months, which was maintained at 6 months. Nielsen et al in 2 studies in 2005 (15) and 2012 (13) and Ahmed et al (16) studied low carbohydrate diet and found reduction in total daily insulin dose in line with our results. Similarly, studies by O'Neill et al (14) and Wong et al, (17) found reduction in total daily insulin dose when applying very low carbohydrate ketogenic diets. This is explained by the fact the bolus insulin dose depends mainly on the carbohydrate content of food which has been restricted in our regimen. Lower carbohydrate consumption meant lower bolus doses and with some weight loss, the total daily doses consequently reduced.

The reduced carbohydrate content caused a reduction in insulin doses, less calculation errors and thereby a decrement in the incidence of hypoglycemic and hyperglycemic events. Also, the fact that some meals and snacks were free of carbohydrates, meant that sometimes no bolus insulin was needed and therefore no risk of hypoglycemia with these meals or snacks. Nielsen et al, 2005, (15) observed a reduction of the total daily insulin dose with low carbohydrate regimens. Merrill et al in a review article concluded reduction of insulin doses in subjects with type 1 diabetes on low carbohydrate diets. (18)

In our study patients lost 5.2% and 7.3% of their baseline body weight after 3 and 6 months of low carbohydrate diets, respectively which resulted in a significant reduction in BMI (-2.1Kg/m^2 after 6 months). Nielsen et al, 2012 found significant reduction in body weight and BMI when applying a low carbohydrate diet in a population of type 1 diabetes cases (13). Scott el al, in a review article also observed weight loss with low carbohydrate diets (2). Another review by Motalib et al, found low carbohydrate diet resulted in weight loss, through both calorie deficit and lower insulin doses. They explain that this is due to an anabolic effect of insulin treatment, or from a higher caloric intake as a result of fear of hypoglycemia. (19)

Our study also showed a significant decline in percent body fat at the end of the 6 months. Studies about percent body fat in type 1 diabetes are scarce. However, Wrzosek et al (20) and Joy et al (21) studied the effect of low carbohydrate-high fat diets, and found that they decreased body fat. Regarding muscle mass, we observed a significant improvement after 6 months of low carbohydrate diet. A study by Rosenfalck et al, demonstrated increased muscle mass in type 1 cases when HbA1c improved. (22) This has been observed elsewhere too, where lean mass was consistently inversely associated with HbA1c and is explained by the fact the hyperglycemia causes catabolism where muscle mass is lost. (23)

In our study, serum triglycerides, serum LDL and total cholesterol have shown a significant decline. The HDL showed a non-significant change. In the literature there have been controversial studies regarding the effect of low carbohydrate, high fat regimens on serum lipids. While Dong et al in a meta-analysis, show a decline in triglycerides (24) Nielsen et al, show a non-significant change (13). Triglyceride reduction has been associated with lower carbohydrate intake especially when monosaccharides intake has been reduced (25).

Dong et al (24) also show that LDL levels rise with low carbohydrate diets and is supported by Kirkpatrick et al.(26) Varady et al shows the opposite(27). O' Neill et al, found a decline in LDL and triglycerides when following low carbohydrate diets. (14) Our results show a significant decline which we attribute to a low carbohydrate not a very low carbohydrate regimen. The percentage of fats in our regimen was only 50%. We also focused on providing unsaturated fat sources (28) and encouraging our subjects to include them in their food regimen. Thus, LDL response cannot be predicted in the individual, and should be evaluated in those who choose to follow a low carbohydrate and very low carbohydrate ketogenic diets.

There was no significant change in HDL, while Dong et al found a significant increase. (24)

The ALT, AST, serum albumin and urinary albumin/creatinine ratio all showed a significant reduction in their values. However, this remains clinically non-significant as all the values were within the normal reference range over the entire study period. A meta-analysis shows that low carbohydrate diet had no influence on liver enzymes (29).

5. Conclusion

This study provides evidence that a low carbohydrate diet is a feasible lifestyle option for adults with type 1 diabetes who fail to achieve glycaemic control despite appropriate carbohydrate counting, adequate self-monitoring and medical supervision, particularly those wishing to lose weight or in need to. It has been found to positively impact type 1 diabetes subjects regarding diabetes control, reduction of total daily insulin dose, reduced risk of hypoglycemic events, weight management, body fat and serum lipids with a good safety profile.

References

1. Krebs JD, Parry Strong A, Cresswell P, Reynolds AN, Hanna A and Haeusler S. A randomised trial of the feasibility of a low carbohydrate diet vs standard carbohydrate counting in adults with type 1 diabetes taking body weight into account. Asia Pacific Journal of Clinical Nutrition. 2016;25(1):78–84
2. Scott SN, Anderson L, Morton JP, Wagenmaker AJM and Riddell MC. Carbohydrate Restriction in Type 1 Diabetes: A Realistic Therapy for Improved Glycaemic Control and Athletic Performance? Nutrients. 2019;11: 1022.
3. Centers for Disease Control and Prevention (CDC).Trends in intake of energy and macronutrients–United States, 1971–2000. 2004; Morbidity Mortality Weekly Report 53, 80–82. 23.
4. Austin GL, Ogden LG and Hill JO. Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese individuals: 1971–2006. American Journal of Clinical Nutrition. 2011; 93: 836–843.
5. Corbin KD, Driscoll KA, Pratley RE, Smith SR, Maahs DM and Mayer-Davis EJ.

Advancing Care for Type 1 Diabetes and Obesity Network (ACT1ON) Obesity in Type 1 Diabetes: Pathophysiology, Clinical Impact and Mechanisms. Endocrinology Revision. 2018; 39: 629–663

6. Petrie JR, Sattar N (2019) Excess cardiovascular risk in type 1 diabetes mellitus. Circulation 139(6):744–747
7. Oh R, Gilani B, Uppaluri KR. Low Carbohydrate Diet. [Updated 2021 Jul 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
8. United states department of agriculture. 2015-2020. Estimated calorie needs per day, by age, sex and physical activity level. Dietary Guidelines for Americans. Appendix 2. Table A2-1.
9. Mehar, S., St John, J., Cheyette, C. and Balolia, Y., Carbs & cals.(World Foods) 1st ed. Great Britain: Chello Publishing. 2019
10. Cheyette, C. and Balolia, Y., Carbs & Cals. (Carb & Calorie Counter) 6th ed. Great Britain: Chello Publishing. 2016
11. American Diabetes Association. Glycemic Targets: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022; 45: S90-S101.
12. Hirsch IB, Brownlee M. Should minimal blood glucose variability become the gold standard of glycemic control? J Diabetes Complications.2005;19(3):178-81.
13. Nielsen JV, Gando C, Joensson E and Paulsson C. Low carbohydrate diet in type 1 diabetes, long-term improvement and adherence: A clinical audit. Diabetology & Metabolic Syndrome .2012; 4(23).
14. O' Neill DF, Westman EC, Bernstein RK. The effects of a low-carbohydrate regimen on glycaemic control and serum lipids in diabetes mellitus. Metabolic Syndrome Related Disorders. 2003; 1(4):291–8.
15. Nielsen JV, Jönsson E, Ivarsson A. A low carbohydrate diet in Type 1 diabetes: Clinical experience--A brief report. Ups J Med Sci. 2005; 110(3):267-73
16. Ahmed SR, Bellamkonda S, Zilbermint M, Wang J, Kalyani RR. Effects of the low carbohydrate, high fat diet on glycemic control and body weight in patients with type 2 diabetes: experience from a community-based cohort BMJ Open Diabetes Research and Care. 2020 ;**8:**e000980.
17. Wong K, Raffray M, Roy-Fleming A, Blunden S, Brazeau AS. Ketogenic Diet as a Normal Way of Eating in Adults With Type 1 and Type 2 Diabetes: A Qualitative Study. Canadian Journal of Diabetes. 2021; 45: 137-143
18. Merrill JD, Soliman D, Kumar N, Lim S, Shariff AI and Yancy Jr WS. Low-Carbohydrate and Very-Low-Carbohydrate Diets in Patients With Diabetes. Diabetes Spectrum.2020; 33(2): 133-142.
19. Motalib A, Kasetty M, JY Mar, Elsaidy T, Ashrafzadeh S and Hamdy O. Weight management in Patient with type 1 diabetes and obesity. Curr Diab Rep.2017;17:92
20. Wrzosek M, Woźniak J,Włodarek D. The effect of high-fat versus high-carb diet on body composition in strength-trained males. Food Science & Nutrition. 2021; 9 (5): 2541-2548
21. Joy JM. Comparative effects of a low-fat diet and a high-fat, ketogenic diet on body composition and athletic performance in recreationally-active males and females. ProQuest Dissertations & Theses Global. 2018; (2120949660).
22. Rosenfalck AM, Almdal T, Hilsted J and Madsbad S. Body composition in adults with type 1 diabetes at onset and during the first year of insulin therapy. Diabetes Medicine.2001;19:417-423
23. Bower JK, Meadows RJ, Foster MC, Foraker RE, Shoben AB.The Association of Percent Body Fat and Lean Mass With HbA1c in US Adults. J Endocr Soc. 2017; 18;1(6):600-608.

24. Dong T, Guo M, Zhang P, Sun G, Chen B. The effects of low-carbohydrate diets on cardiovascular risk factors: A meta-analysis. PLoS One. 2020; 15(1):e0225348.
25. Parks, EJ, Hellerstein MK Carbohydrate-induced hypertriacylglycerolemia: historical perspective and review of biological mechanisms, The American Journal of Clinical Nutrition.2000;71 (2): 412–433
26. Kirkpatrick CF, Bolick JP, Kris-Etherton PM, Sikand G, Aspry KE, Soffer DE et al.Review of current evidence and clinical recommendations on the effects of low-carbohydrate and very-low-carbohydrate (including ketogenic) diets for the management of body weight and other cardiometabolic risk factors: A scientific statement from the National Lipid Association Nutrition and Lifestyle Task Force. J Clin Lipidol. 2019; 13(5):689-711
27. Varady KA, Bhutani S, Klempel MC, Kroeger CM. Comparison of effects of diet versus exercise weight loss regimens on LDL and HDL particle size in obese adults. Lipids Health Dis. 2011;10:119.
28. Di Nicolantonio JJ, O'Keefe JH. Effects of dietary fats on blood lipids: a review of direct comparison trials.Open Heart. 2018; 5:e000871
29. Haghighatdoost F, Salehi-Abargouei A, Surkan PJ, Azadbakht L. The effects of low carbohydrate diets on liver function tests in nonalcoholic fatty liver disease: A systematic review and meta-analysis of clinical trials. J Res Med Sci. 2016 Jul 29;21:53.