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Effect of Apple Cider Vinegar in Type 2 Diabetic Patients with Poor Glycemic Control: A Randomized Placebo Controlled Design®

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ABSTRACT

Aim: *The aim of the trial was to measure the effect of apple cider vinegar on glycemic control and biochemical parameters in type 2 diabetes mellitus (DM) patients with poor glycemic control.* ***Methods:*** *A single-blind, randomized, placebo-controlled trial was conducted on 110 eligible types 2 DM patients who were selected and allocated into 2 groups. The interventional group was given 15 ml apple cider vinegar in 200 ml water during dinner for 3 months while the other group was placebo. Before and after HbA1C (glycosylated hemoglobin), fasting lipid profile, fasting blood sugar, anthropometrics, and dietary changes were assessed and analyzed using IBM SPSS version 20, through statistical tests. Formal ethical approval was obtained from the local institutional review board.* ***Results:*** *Significant mean change was found in interventional group in HbA1c ($p<0.001$), blood sugar fasting ($p<0.001$), total cholesterol ($p=0.002$), triglyceride ($p=0.002$) and hip-waist ratio ($p=0.002$). No significant change was observed in the mean of these statistics in the placebo group. No significant change was observed in height, weight, mid-upper arm ratio, and low density lipoprotein, high density lipoprotein and food frequency in intervention and placebo groups before and after.* ***Conclusion:*** *Apple cider vinegar if used regularly is effective in controlling diabetes, lowering hypercholesterolemia and hypertriglyceridemia in DM type 2 patients.*

Keywords: Vinegar, Diabetes, Hyperglycemia, Hypercholesterolemia, Nutraceutical

Abbreviations: DM: Diabetes Mellitus; T2DM: Type 2 Diabetes Mellitus; ACV: Apple Cider Vinegar; HbA1c: A form of Hemoglobin (a blood Pigment that carries oxygen); LDL: Low Density Lipoproteins; HDL: High Density Lipoproteins; TC: Total Cholesterol; TG: Total Triglyceride; BMI: Body Mass Index; BSF: Blood Sugar Fasting; RCT: Randomized Control Trail; WHO: World Health Organization; SD: Standard Deviation; SPSS: Social Packages Statistical Software

INTRODUCTION

Diabetes mellitus (DM) has been considered globally as a major public health problem linked with changing life style, reduced physical activity and obesity [1]. Development of diabetes mellitus is due to endocrine disorders which cause

impaired insulin secretion, hepatic glucose over production and insulin resistance. Complications can occur along with co-morbidities such as dyslipidemia, atherosclerosis, and hypertension [2].

World Health Organization (WHO) predicted DM to be the 7th cause of mortality by the year 2030 [3]. The 2013 estimates of the International Diabetes Federation (IDF) showed that about 382 million people globally have diabetes, and it will increase to 592 million by the year 2035. About 80% of populations with diabetes are from poor socio-economic countries and 60% of them are from Asia whereas, one-third is from China. In developing countries, the rapid rise of type 2 DM is observed [4]. Prevalence of diabetes mellitus is found to be high in south Asian developing countries and India is topping the list. Pakistan is also facing a progressive increase in the diabetes burden. National level surveys showed DM prevalence of 13.14% in Punjab and 13.9% in Sindh [5].

Food additives which are grown by natural origin have been more popular in recent year for treating the diseases even without showing evidence of medical benefits. The ethnic, cultural and religious belief of various communities and easy access to internet information enhanced their preference for natural treatment remedies for various diseases [6]. Natural products have fewer side effects as compared to medical therapies, as perceived by the general population. Diabetics are 1.6 times more likely to use alternative medical products and complementary food than non-diabetics individuals [7]. Obese individuals are more likely to use alternative products or dietary supplements for reduction of their body weight and to gain other beneficial metabolic effects [6].

The word vinegar is derived from French word "*vin aigre*" meaning sour and it can be made almost from any fermentable sugar (carbohydrate) source such as apple, dates, grapes, and sorghum, etc. Acetic acid is an active component in apple cider vinegar responsible for its pungent, biting odour and tart flavour containing to 3%-9% acidity [2]. Apple cider vinegar is produced by fermenting apples in the form of an acidic solution. Its contain minerals, vitamins, and other trace elements and vinegar also contains a potent supply of potassium, as potassium is essential for the replacement of worn-out tissues within the body and repair of soft tissue [8].

Apple cider vinegar has beneficial effects in the treatment of endocrinal, gastrointestinal, renal, neurological, nasal, joints, cardiovascular and muscular disorders and many skin infections. Some studies reports showed that vinegar affects the glucose and insulin responses to a sucrose or starch load [8]. Acetic acid is the active component in apple cider vinegar which affects blood glucose metabolism and many other mechanisms which contribute to explain antiglycemic effects of vinegar. The mechanism by which vinegar reduces glucose levels are still unclear, acetic acid may slow gastric emptying [9]. Alternatively, acetic acid may inhibit disaccharides activity in the small intestine blocking the complete digestion of starch molecules and also promotes skeletal muscles glucose uptake in the body [10,11].

Vinegar usage improves hyperinsulinaemia, hypertriglyceridaemia, insulin sensitivity and can also reduce the level of random blood glucose in diabetic patients as well as in healthy individuals [12]. Evidence of many studies showed that a single dose of vinegar (20 g) with 5% acidity can decrease PPG (post prandial glucose) in diabetic as well as in healthy individuals by 50% [6,13]. This study showed that apple cider has anti-diabetic, anti-hyperlipidemic and anti-obesity effects in diabetes mellitus [6]. Insulin response and postprandial glucose can be influenced by type and dose of vinegar [13-15].

A randomized control trial (RCT) showed two different concentration of vinegar, 0.16%, and 1.6% found to be effective on 7th days of intervention onwards but not after 3rd day [8]. Many clinical trials found that apple cider vinegar can reduce obesity, hyperglycemia, hyperlipidemia, and hyperinsulinaemia. Emphasizing that apple vinegar is helpful for diabetes management as a complementary agent in diet [16,17].

A study conducted in pre-diabetic healthy individuals showed significant ($p=0.05$) reduction in HbA1C, in apple cider vinegar group [18]. Many RCTs of human and animals showed the hypolipidemic effects of ACV [19-21]. Anti-obesity effect of apple cider vinegar is also found in many studies [22-24]. There is still a lot of research trials on the effectiveness of apple cider vinegar in different sets of the population of diabetes. The aim of the trial was to measure the effect of apple cider vinegar on glycemic control and biochemical parameters in type 2 DM patients with poor glycemic control attending a tertiary care hospital in Lahore, Pakistan.

METHODOLOGY

Study Design and Setting

This study was a single-blind, placebo controlled trial. Parallel design using 1:1 allocation ratio was used. This clinical

trial was registered www.clinicaltrials.gov and also follows the CONSORT guidelines and prepared the CONSORT checklist.

Participants

Adult patients having type 2 diabetes mellitus, of both genders within the age group from 30-60 years were included in the study. All having body mass index between 20-30 kg/m^2, non-smoker and non-alcoholics and all were on standard medical therapy for diabetes, tablet TagipMet (Metformin+Sitagliptin group). To maintain the uniformity (Metformin plus sitagliptin) drug receiving patients were selected and secondly, this drug was commonly prescribed by physician among the Pakistani population. To avoid discrepancy of results single and same drug user patients were selected. Patients suffering from known chronic renal disease and history of cardiovascular diseases, stroke, ischemic heart disease, and known allergy or intolerance to vinegar, reported by the patient or relative and any kind of acute infection were excluded from the study (Figure 1).

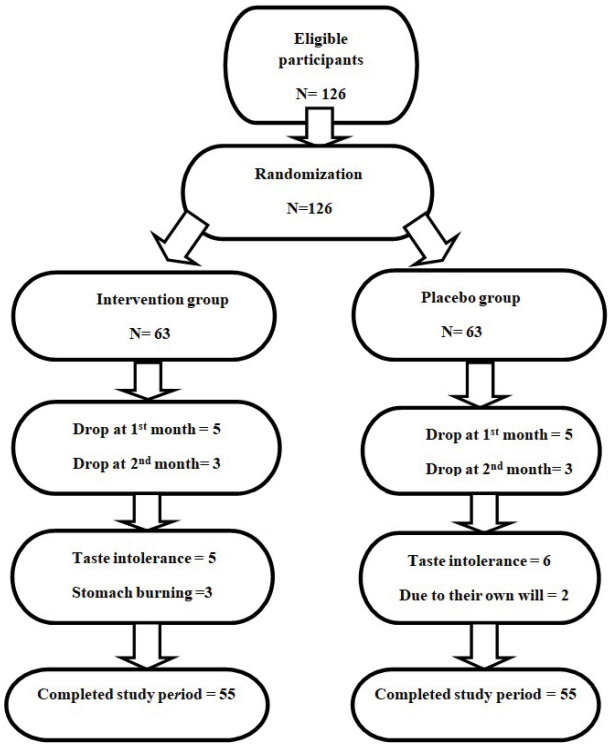

Figure 1 Flow diagram of study participants

The trial period was 3 months from August 15, 2017, to November 15, 2017. This study was conducted at a 1050 bed, tertiary care, and teaching hospital of Lahore, Pakistan. This hospital has high diabetes mellitus out-patient turnover as a reputable center in the management of diabetes.

Intervention

Experimental: intervention group: Intervention group patients taking their diet according to their original meal pattern only dietary instruction in the view of (American diabetic association dietary guideline) were given regarding high glycemic and low glycemic diet (which diet should be helpful for controlling diabetes) [25]. Medical treatments continued (including tablet TagipMet 50 mg or 1000 mg twice a day) (Metformin+Sitagliptin group). About 15 ml apple cider vinegar (American garden organic vinegar) (containing 5% acetic acid as verified/approved by food drug authority) was mixed in 200 ml water during a meal at night time was prescribed [2].

Placebo comparator: comparison group: Control group also taking their diet according to their original meal pattern only dietary instruction in the view of (American diabetic association dietary guideline) were given regarding high glycemic and low glycemic diet (which diet should be helpful for controlling diabetes) [25]. Medical treatment continued (including Tablet TagipMet 50 mg or 1000 mg twice a day) (Metformin+Sitagliptin group). About 15 ml

artificial flavor of apple cider vinegar was mixed in 200 ml plain water during a meal at night time was used as a placebo [2].

Outcome Measure (Dependent Variables)

Primary outcome measure:

- HbA1c (glycosylated hemoglobin): Before the start of intervention and after intervention 5 ml venous blood sample was taken for biochemical analysis of HbA1C (glycosylated hemoglobin) in sterilized tubes, commercial kits of Siemens for Dimension RXL used and the HbA1C measurement is based on a turbidimetric inhibition immunoassay (TINIA) principle

Secondary outcome measures:

- Blood sugar fasting (BSF): Before the start of intervention and after intervention 5 ml venous blood sample was taken with 12 hours fasting for biochemical analysis of blood sugar fasting in sterilized dray tubes, commercial kits of Siemens for Dimension XL and photometric methods for analysis was used
- Fasting lipid profile: Before the start of intervention and after intervention 5 ml venous blood sample was taken with 12 hours fasting for biochemical analysis of fasting lipid profile commercial kits of Rodex for Dimension RXL and photometric methods for analysis were used
- Anthropometric measurements: Height was measured in centimeter to nearest 0.1 cm by using standard stadiometer before intervention and weight was measured in kilogram to nearest 100 g with wearing light cloth by using a calibrated weighing scale machine before and after the intervention. Hip/waist ratio and mid upper arm were measured with measuring tape in centimeter to nearest 0.1 cm. The BMI of study participants were classified as underweight, normal, over weight and obese according to WHO criteria weight was measured as weight/height (kg/m^2) [26]

Confounding Variables

Dietary intake: Diet of study participants can influence and confound the intervention during the study period so it was assessed through a food frequency questionnaire. Food frequency was filled 2 times before and after the intervention to measure change during the study period which can actually confound the effect of apple cider vinegar. The food frequency questionnaire (FFQ) was structured according to Pakistan's cultural food preferences and choices. FFQs contained methods of food preparation, frequency per day and per week and portion size/amount of food consumed in categories from never, monthly to 1-7 days in a week. Food exchange lists were used to assess the portion size of food. FFQ was composed of cereal group, fruits, vegetable, meat, milk, fat/oil, snacks, and beverages.

Independent Variable/Intervention

This selected nutraceutical (apple cider vinegar) was given for 3 months. Apple cider vinegar was provided to patients and instructions were given to all participants about the uses of apple cider vinegar.

Sample Size

The sample size of 110 (55 in each group) was estimated by using 95% confidence level, 80% power with an expected mean change in HbA1c 0.53% and 0.11% for cases treated with apple vinegar and placebo respectively with a SD of 0.77% (by using power+precision 3.0 software) [2]. Assuming a 12.6% non-response rate, RCT started with 126 patients, 63 patients in each group. Total 16 patients were lost to follow up during the study period, so finally statistical analysis was done on 110 patients 55 in each group.

Randomization

Principal researcher/investigator approached participants in the outpatient department and after determining their eligibility they were allocated using the lottery method to a group, intervention or placebo.

Implementation

The trial period was 3 months. Randomization of all participants was done and intervention was started from August 15, 2017, and ended on November 15, 2017.

Blinding

All study participants were blinded regarding the intervention of apple cider vinegar and placebo but the investigator was not blind.

Statistical Analysis

Descriptive statistical analysis was done for the demographic profile, categorical and numerical variables by measuring frequency, percentage, the mean and standard deviation of all samples. Paired sample T-test was used for anthropometrics measurement and biochemical assessment for 2 time assessment before and after intervention for both the groups (between groups). One-way ANOVA was used for comparison within the groups. McNemar statistical test was used to assess the food frequency questionnaire before and after the intervention.

Ethical Considerations

Proper ethical clearance was obtained from local Institutional Review Board. (Approval of Technical Research Committee and Institutional Review Board of Federal post graduate medical institute Shaikh Zayed Hospital Lahore Pakistan, National Health Research Complex, National Institute of Kidney Diseases, National Institute of Nursing Allied Sciences, approval letter number was 1418).

RESULTS

Statistical Analysis

Demographics and social factors: The mean age of patients in the intervention group was 51.1636 ± 7.91568 ranging from 30-60 years. The mean age of patients in the placebo group was 50.4909 ± 7.78382 ranging from 30-60 years. In the intervention group, 34 (61.8%) were females while in placebo group 29 (52.7%) were female. In the current study, 29.1% of patients were illiterate in the intervention group while 14.5% were illiterate in placebo group followed by other categories of literacy. Occupational status of study participants in the intervention and placebo group is shown in Table 1. Frequency and percentage of age, gender, educational status and occupational status of intervention and placebo group has been described in Table 1.

Table 1 Demographic characteristic of study participants

Intervention Group		Placebo Group	
Characteristics	**Percent**	**Characteristics**	**Percent**
Age (Years)			
30-40	14.5%	30-40	14.5%
41-50	30.9%	41-50	30.9%
51-60	54.5%	51-60	54.5%
Gender			
Male	38.2%	Male	47.3%
Female	61.8%	Female	52.7%
Educational Status			
Illiterate	29.1%	Illiterate	14.5%
Middle	10.9%	Middle	21.8%
Metric	23.6%	Metric	21.8%
Intermediate	18.2%	Intermediate	29.1%
Graduate	12.7%	Graduate	10.9%
Above graduate	5.5%	Above graduate	1.9%
Occupational Status			
Medical	5.5%	Medical	12.7%
Teaching	18.2%	Teaching	10.9%
Other	76.4%	Other	76.4%

Medication, diet and test material adherence/compliance: About 38.2% of participants were strictly following their prescribed medication, 45.5% moderately and 16.3% irregularly compliant in the intervention group. In the placebo group, 27.3% participants were strictly following their prescribed medication, 56.4% were moderately following and 16.3% were irregularly compliant. About 8 (14.5%) patients were strictly following their prescribed

diet plan, 37 (67.3%) were moderately following and 10 (18.2%) patients were irregular in their diet plan follow up in the intervention group. 12 (21.8%) participants were strictly following their prescribed diet plan, 34 (61.8%) were moderately and 9 (16.4%) patients were irregularly compliant in the placebo group. Apple cider vinegar strictly used by patients was 21 (38.2%), moderately used were 20 (36.4%) and irregular were 14 (25.5%) in intervene group. Total 16 (29.1%) strictly follow placebo, moderately follower was 26 (47.3%) and irregular follower was 13 (23.6%) in the placebo group (Table 2).

Co-morbidities and complications: Among complications of diabetes, the visual problem was 74.5% in intervention group and 60.0% in the placebo group. About 49.1% of participants in the intervention group were hypertensive as compared to 38.2% in the placebo group. Neuropathy with diabetes was found in 50.9% in intervention group and 43.6% in the placebo group. Frequency and percentage of diabetes and co-morbidity, life style, diet, medication, test material and placebo material of intervention and placebo group has been described in Table 2.

Table 2 Diabetes, co-morbidities and life style activities

Intervention Group			Placebo Group		
Characteristics		**Percent**	**Characteristics**		**Percent**
Vision problem	Yes	74.5%	Vision problem	Yes	60.0%
	No	25.5%		No	40.0%
Blood pressure	Yes	49.1%	Blood pressure	Yes	38.2%
	No	50.9%		No	61.8%
Neuropathy	Yes	50.9%	Neuropathy	Yes	43.6%
	No	49.1%		No	56.4%
Physical activities	Heavy	5.5%	Physical activities	Heavy	12.7%
	Moderate	67.3%		Moderate	56.4%
	Light	27.3%		Light	30.9%
Exercise	Daily	1.8%	Exercise	Daily	5.5%
	Once in Week	18.2%		Once in Week	9.1%
	Monthly	5.5%		Monthly	10.9%
	Never	74.5%		Never	74.5%
Walk	Half Hour	54.5%	Walk	Half Hour	54.5%
	1 Hour	20.0%		1 Hour	9.1%
	None	25.5%		None	36.4%
Sleeping	Below 5 hours	9.0%	Sleeping	Below 5 hours	3.6%
	5-7hours	20.1%		5-7hours	41.8%
	above 7 hours	70.9%		above 7 hours	54.5%
Medication Follow up	Strictly Follow	38.2%	Medication Follow up	Strictly Follow	27.3%
	Moderately Follow	45.5%		Moderately Follow	56.4%
	Irregular	16.3%		Irregular	16.3%
Diet plan Follow up	Strictly Follow	14.5%	Diet plan Follow up	Strictly Follow	21.8%
	Moderately Follow	67.3%		Moderately Follow	61.8%
	Irregular	18.2%		Irregular	16.4%
Apple cider vinegar follow up	Strictly Follow	38.2%	Placebo follow up	Strictly Follow	29.1%
	Moderately Follow	36.4%		Moderately Follow	47.3%
	Irregular	25.5%		Irregular	23.6%

Anthropometric measurements: On paired sample T-test no significant change was found in intervention and placebo groups for height, weight and mid arm circumference, before and after intervention were seen. A significant change in mean for hip waist ratio was found in the intervention group before intervention (BI) mean of 37.9 ± 2.74 SD and after intervention (AI) mean ± SD 37.5 ± 3.09 and p=0.002. No significant change was found in the placebo group (Table 3). One-way ANOVAs for anthropometric measurements within groups showed insignificant findings.

Table 3 Anthropometric and biochemical measurements

Intervention Group			Placebo Group		
Characteristics	**Mean ± SD**	**p-values**	**Characteristics**	**Mean ± SD**	**p-values**

Height before	162.83 ± 8.66	0.322	Height before	161.18 ± 10.91	0.322
Height after	162.83 ± 8.66		Height after	161.54 ± 10.90	
Weight before	72.38 ± 10.59	0.164	Weight before	71.76 ± 11.53	0.255
Weight after	72.07 ± 10.81		Weight after	71.85 ± 11.56	
MUA circumference before	11.30 ± 1.95	0.033	MUA circumference before	11.38 ± 2.08	0.322
MUA circumference after	11.09 ± 1.97		MUA circumference after	11.40 ± 2.07	
H/W circumference before	37.90 ± 2.74	0.002	H/W circumference before	37.76 ± 3.46	0.060
H/W circumference after	37.50 ± 3.09		H/W circumference after	37.92 ± 3.47	
HBA1C before	9.32 ± 1.74	0.000	HBA1C before	9.07 ± 1.76	0.206
HbA1C after	8.65 ± 1.81		HbA1C after	10.71 ± 9.41	
BSF before	170.14 ± 62.42	0.000	Blood sugar fasting before	170.36 ± 66.18	0.034
BSF after	157.32 ± 58.16		Blood sugar fasting after	170.81 ± 65.99	
Total cholesterol before	195.81 ± 47.97	0.002	Total cholesterol before	190.18 ± 68.06	0.057
Total cholesterol after	180.09 ± 48.59		Total cholesterol after	192.92 ± 68.46	
HDL before	43.49 ± 11.29	0.112	HDL before	49.69 ± 24.66	0.014
HDL after	45.70 ± 8.23		HDL after	49.10 ± 24.61	
LDL before	121.66 ± 38.10	0.030	LDL before	108.05 ± 37.44	0.129
LDL After	114.18 ± 39.60		LDL after	111.16 ± 40.67	
Triglyceride before	192.21 ± 77.98	0.002	Triglyceride before	185.32 ± 87.40	0.036
Triglyceride after	180.27 ± 79.67		Triglyceride after	197.14 ± 83.68	
Level of significance ($p<0.05$); Intervention group hip/waist ratio $p<0.002$; Intervention group HbA1C $p<0.001$; Intervention group Blood sugar fasting $p<0.001$; Intervention group total cholesterol $p<0.002$; Triglyceride intervention group $p<0.002$					

Biochemical assessments: Paired sample T-test results showed that HbA1C and blood sugar fasting significantly changed in intervene group after apple cider vinegar intervention of 3 months. HbA1C before intervention (BI) mean was 9.32 ± 1.74 SD and AI mean was 8.65 ± 1.81 SD with $p<0.001$. BSF BI mean was 170.14 ± 62.42 SD, while BSF after intervention (AI) mean was 157.32 ± 58.16 SD with $p<0.001$. No significant change in HbA1C and BSF was found in before and after in placebo group (Figure 2).

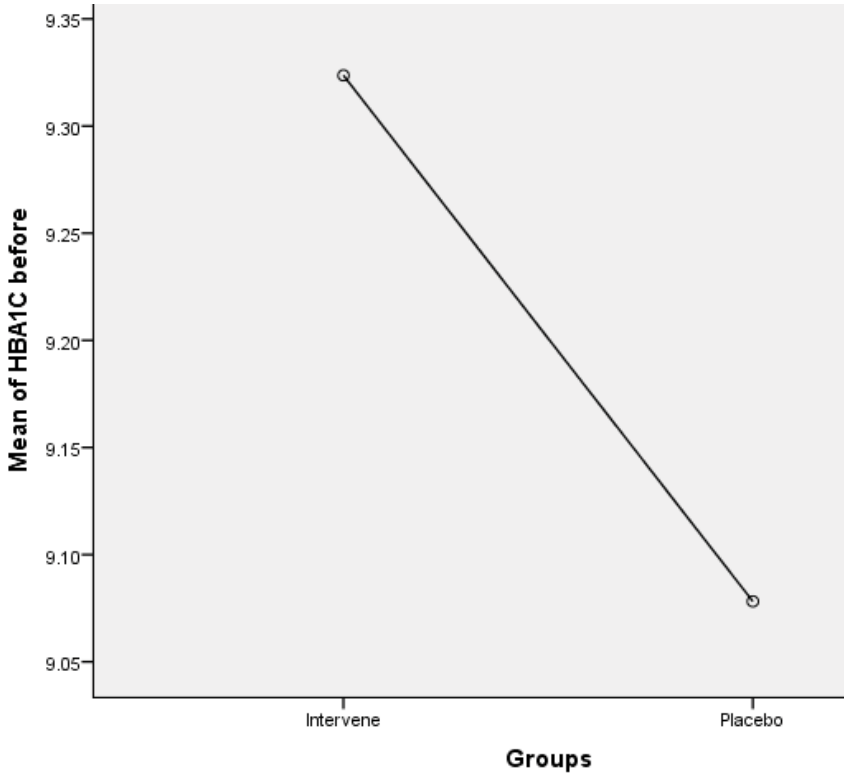

Figure 2 Mean plot chart of HbA1c before the intervention of intervention and placebo groups

Total cholesterol was significantly changed in the intervention group, with a mean difference of total cholesterol BI means was 195.81 ± 47.9 SD and AI mean was 180.09 ± 48.5 SD with p=0.002. But there was no significant change in the placebo group. Triglyceride significantly changed in the intervention group with mean difference BI was 192.2 ± 77.9 AI was 180.2 ± 79.6 with p=0.002. There was no significant change in the placebo group. High density lipoprotein (HDL) was not significantly changed in both groups. No significant change was found in both groups for low density lipoprotein (LDL) (Table 3). One-way ANOVAs for biochemical assessments within groups showed insignificant findings.

Confounder variables including (age, gender, occupation, education, physical activity, exercise, walk, and sleeping) were also measured by using regression model so, no significant effect of confounder variables on dependant variable (HbA1C) was found after an interventional period of both groups (Table 4 and Figure 3).

Table 4 Confounders' effect on HbA1C

Groups	Models	Unstandardized Coefficients		Standardized coefficients	Tail	p-values
		B	St error	Beta		
Intervene	Constant	9.172	2.966	-	3.092	0.003
	Age	0.454	0.357	0.173	1.271	0.210
	Gender	0.825	0.531	0.223	1.552	0.127
	Occupation	-0.334	0.462	-0.104	-0.723	0.473
	Education	0.235	0.174	0.205	1.349	0.184
	Physical activity	0.407	0.427	0.120	0.954	0.345
	Exercise	0.229	0.196	0.158	1.169	0.248
	Walk	-0.431	0.184	-0.299	-2.340	0.024
	Sleeping	-1.365	0.555	-0.304	-2.459	0.018
Placebo	Constant	34.385	14.216	-	2.419	0.020
	Age	-2.988	1.900	-0.233	-1.573	0.123
	Gender	-1.178	2.909	-0.063	-0.405	0.687
	Occupation	-0.874	2.059	-0.065	-0.424	0.673
	Education	-2.129	1.199	-0.297	-1.775	0.083
	Physical activity	-2.141	2.132	-0.146	-1.004	0.321
	Exercise	-0.073	1.142	-0.009	-0.064	0.950
	Walk	-1.211	0.963	-0.182	-1.258	0.215
	Sleeping	0.692	2.541	0.042	0.273	0.786

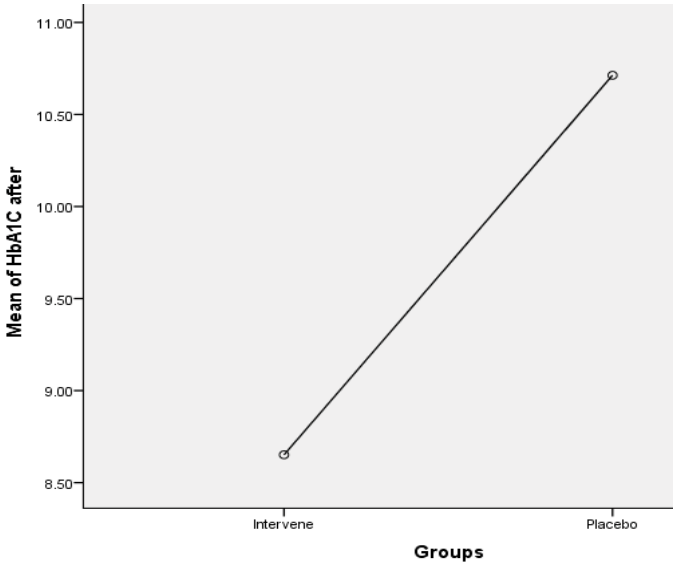

Figure 3 Mean plot chart of HbA1c after the intervention of intervention and placebo groups

DISCUSSION

In intervention and placebo groups, the mean age was not much different (51.1 ± 7.9 and 50.4 ± 7.7 respectively) with female predominance in both (61.8% in intervention group and 52.7% in placebo). A study conducted in Iran showed a similar demographical picture of study participants but with different sample size [2,23]. The current study showed complications of diabetes including visual problem, neuropathy, and hypertension. While few studies documented no complication in early diagnosed type 2 diabetic patients [18].

In the current study no significant change found in height, weight and mid upper arms circumference in both groups before and after. Hip/waist ratio significantly reduced after intervention (p=0.002) but no significant difference found in the placebo group (p=0.06). A study conducted in Japanese showed apple cider vinegar significantly reduced bodyweight, waist circumference, and BMI in vinegar treated group as compared to placebo [23]. Another animal study results highlighted significant reduction in daily gained and in routine body weight in normal healthy rats with normal diet and in obese rats with high calories diet in vinegar treated group but no significant change occurred in the placebo group [24]. The reason for the reduction in body weight and BMI may be due to the difference in the physiology of human and animals and dose of vinegar, duration of intervention and sample size.

In current study HbA1C and blood sugar fasting were significantly reduced in the intervention group, HbA1C (p<0.001), blood sugar fasting (p<0.001) no significant difference in mean of HbA1C, BSF in the placebo group. Previous study results showed HbA1C (p=0.002) and BSF (p=0.006) significantly reduced in the intervention group but not significantly changed in these parameters of the placebo group [2]. Another study showed a significant reduction in fasting blood sugar (p=0.05), in vinegar (750 mg) ingestion group when compared with vinegar pills (40 mg acetic acid) as control group after 12 weeks trail but no significant change in Hb1C and post prandial glucose was found [18].

The results of the current study showed vinegar had a hypercholesterolemic and hypotriglyceridemic effect. Total cholesterol and triglyceride were significantly reduced in the intervention group (total cholesterol, p=0.002, and triglyceride, p=0.002), no significant change in the placebo group. An animal study showed that dietary acetic acid had efficacy to reduced hypercholesterolemia and hypertriglyceridaemia in vinegar ingestion group of rats but not in the placebo group [27].

HDL and LDL remained the same before and after intervention in intervention and placebo group. A study showed no significant difference in total cholesterol, total triglyceride LDL and HDL after one month intervention of white vinegar as compared to the placebo group [2]. The reason for the insignificant effect of vinegar on hyperlipidaemia could be a short duration of the intervention. Another animal study showed a significant change in blood glucose, total cholesterol, LDL and HDL by indigestion of apple, coconut, grape, sugarcane and palm vinegar with apple cider vinegar most effective in triglyceride, LDL and glucose with 15% concentration for 6 weeks (p=0.005) [28]. Total cholesterol, triglyceride, LDL significantly reduced and HDL also increased but not significantly in hyperlipidemic patients in another study [19].

In the current study before and after intervention in groups, diet remained the same no significant difference was found in any food component before and after. Human subjects study results showed that diet should remain the same before and after the intervention of acetic acid in type 2 diabetic patients to ensure comparability [16].

Confounder variables including (age, gender, occupation, education, physical activity, exercise, walk, and sleeping) were found to have no effect on dependant variable (HbA1C) in both groups. A study conducted on human subjects showed physical activities and life style remained the same before and after the invention and no significant effect of these confounders was found [2]. The current limitation was a small sample size and financial constrains because this study was conducted without funding by any national and international organization. One-way ANOVAs (analysis of variance) for anthropometric measurements and biochemical assessments within groups showed insignificant findings.

CONCLUSION

The current study concludes that apple cider vinegar had a positive effect on controlling diabetes in diabetic patients and lowering hypercholesterolemia and hypertriglyceridemia. HbA1C, fasting blood glucose, total cholesterol, and triglyceride, and hip/waist circumference values were significantly reduced in the intervened group after 3 months

of apple cider vinegar intervention. No significant change occurred in the values of LDL, HDL and body weight. Physical activities, adequate sleep, diet plan follow up, adherence to prescribed medication and use of apple cider vinegar as a nutraceutical can be beneficial in reducing HbA1C, hypercholesterolemia, and hypertriglyceridemia in type 2 diabetic patients.

DECLARATIONS

Trial Registration

This clinical trial has been registered at www.clinicaltrials.gov, retrospectively, trial registration #NCT03593135, on 18th July 2018.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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