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Effects of a Healthy Diet plus Peanut Consumption on the Fasting Lipid Profile of HIV-infected Adults in Nyeri County, Kenya: A Randomized Crossover Study

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ARTICLEINFO	ABSTRACT
	Introduction: Dyslipidemia is a key modifiable cardiovascular risk factor and a major clinical feature in the patients infected with the human immunodeficiency virus (HIV) in the current era of highly active antiretroviral therapy. Peanuts could reduce the risk of cardiovascular diseases as an abundant source of fiber, α-tocopherol, copper, arginine, magnesium, folate, and resveratrol. The present study aimed to evaluate the impact of supplementing peanut and counseling in the form of a healthy diet on the fasting lipid profile of HIV-infected adults. **Methods:** This randomized crossover clinical trial was conducted on the eligible participants who were randomly assigned to a two-arm study. In treatment I, the participants consumed 80 grams of peanuts plus their regular diet. In treatment II, the participants were provided with nutrition counseling on a healthy diet and consumed 80 grams of peanuts. Each treatment continued for eight weeks with a six-week washout interval. **Results:** A 3.07% reduction was observed in the total cholesterol of the subjects receiving treatment I, while the reduction rate was 5.39% in treatment II. In addition, a 12.8% decrease was observed in the triglycerides of the subjects receiving treatment 1I, as well as a 17% reduction in treatment II. A significant increase was reported in the high-density lipoprotein cholesterol in treatments I and II, with the rate estimated at 7.38% and 5.1%, respectively. Furthermore, low-density lipoprotein cholesterol decreased by 5.56% in treatment I and 4.32% in treatment II. The estimated 10-year risk of contracting coronary heart disease reduced significantly between the baseline and end of the study (P=0.03). **Conclusion:** According to the results, regular consumption of peanuts could improve the fasting lipid profile of HIV-infected patients and reduce the risk of coronary heart disease.

Introduction

The burden of cardiometabolic diseases is growing in Sub-Saharan Africa (SSA) as the landscape of the human immunodeficiency virus (HIV) care changes, [1] and the cardiovascular disease mortality rate is expected to double to 2.4 million by 2030 relative to reports in 2000. [2] Evidence suggests that cardiometabolic diseases would become a key health concern in SSA, competing for limited health resources with infectious diseases. [3]

Cardiovascular diseases (CVDs) are currently the second most common cause of death after cancer in the populations living with HIV in the regions of the world where highly active antiretroviral therapy (HAART) is widely available. [4]

Dyslipidemia associated with HAART is a prevalent condition in the patients living with HIV. Above 85% of the patients infected with HIV who receive HAART currently survive for more than 10 years after acquiring the infection. [5] On the other hand, the significant increase in life expectancy coupled with the reduction of morbidity and mortality as a result of HAART have been accompanied by the increased rate of clinical and metabolic complications. Some of these metabolic complications include dyslipidemia, hyperinsulinemia, and adipose tissue distribution. [6]

Dyslipidemia is a key modifiable cardiovascular risk factor and a major clinical feature of HIV-infected patients in the current era of HAART. [7] Non-pharmaceutical interventions such as diet

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and physical exercise should be the first-line intervention for the management of dyslipidemia. [8] Other interventions include reduced calorie intake, achieving an ideal bodyweight, and increasing physical activity. These first steps may yield added health benefits in HIV-related dyslipidemia. [9] In an HIV-uninfected population, dietary counseling may respectively result in 11% and 22% reduction of cholesterol and triglyceride (TG), while in HIV-infected individuals, the reduction rate may be 4-17% and 21-26%, respectively. [10] A study conducted by Barrios et al. [11] aimed to prospectively evaluate the impact of a low-fat diet on the reduction of cholesterol and TG in 230 HIV-infected individuals, and it was reported that proper dietary adherence resulted in 11% and 10% reduction of the total serum cholesterol and

12% and 23% in the serum TG after three and six months, respectively.

Peanuts could reduce the risk of CVDs as an abundant source of fiber, α-tocopherol, copper, arginine, magnesium, folate, and resveratrol. Therefore, regular consumption of peanuts might benefit high-risk individuals for CVDs. The available studies on the effects of peanuts have only been performed on healthy adults or patients with diabetic dyslipidemia based on a fat-restricted diet.

The present study aimed to investigate the effects of dietary counseling and peanut supplementation on the serum lipid profile of normal HIV-infected adults and those with hyperlipidemia referring to the comprehensive care clinics in Nyeri Level-5 Hospital.
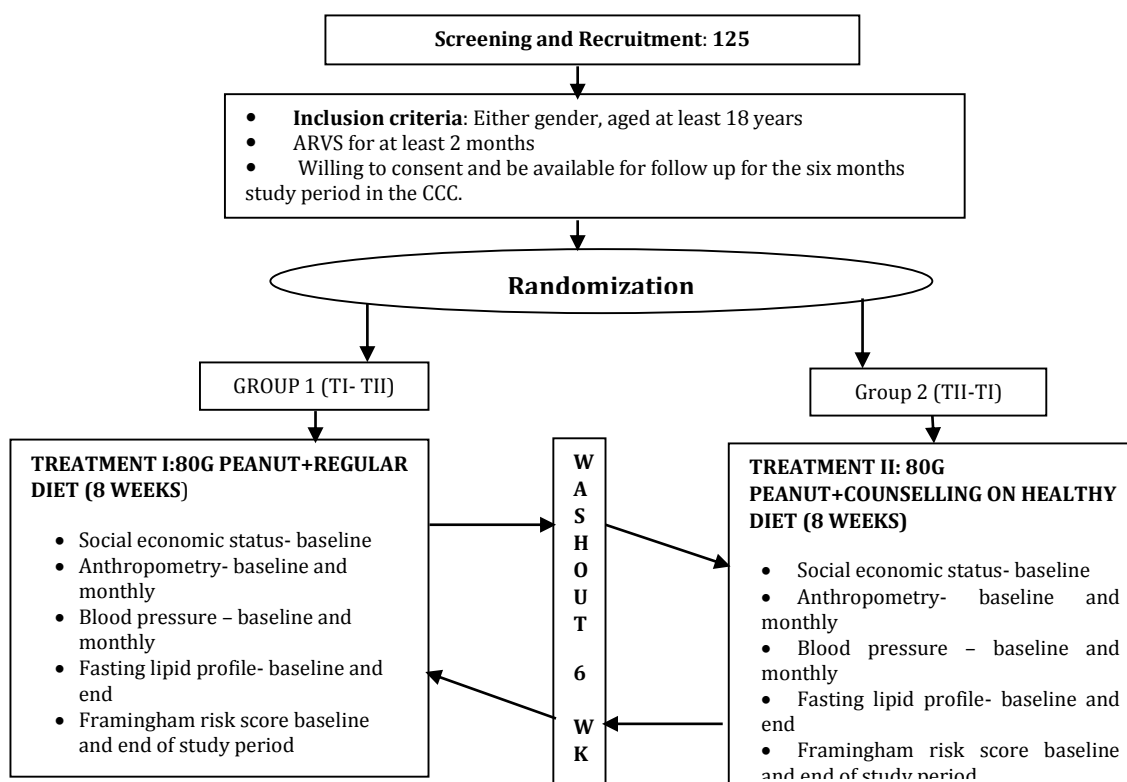
Figure 1. Intervention procedure

Materials and Methods

This randomized crossover clinical trial was conducted on the eligible participants who were randomly assigned to a two-arm study. In treatment I, the participants consumed 80 grams of peanuts plus their regular diet. In treatment II,

the participants were provided with nutrition counseling on a healthy diet and consumed 80 grams of peanuts. Each treatment continued for eight weeks with a six-week washout interval.

The sample population included male and female outpatients aged at least 18 years with a normal

lipid profile or hyperlipidemia. In addition, the patients had to have been receiving antiretroviral drugs for a minimum of two months and willing to be available for a six-month follow-up at the comprehensive care center. The exclusion criteria were as follows: 1) known hypersensitivity to peanuts; 2) allergic reactions to peanuts after a skin test performed by a clinician; 3) pregnant and breastfeeding women; 4) receiving lipid-lowering therapies; 5) performing rigorous exercise; 6) history of diverticulitis or irritable bowel disease that could be deteriorated by daily peanut intake; 7) habitual peanut/tree nut consumers who were unwilling to discontinue the intake of peanut and/or tree nuts for six weeks prior to their first scheduled clinic visit and 8) renal and liver diseases and/or severe dyslipidemia (TG>4.52 mmol/l or TC>7.77 mmol/l).

Sample size was determined using the Fischer equation adopted by Chow Shao and Wang. [12] The sample size had a balanced, crossover design analyzed by t-test, and the probability of type I error (significance level) was estimated at 1.96, while the probability of type II error (test power) was 1.282.

In addition, the expected variance for LDL- C (σ_m^2) was 0.074. [19] When these values were substituted in the formula, the sample size was approximately 38 for each group considering the attrition rate of 20% and a total of 91 participants.

Randomization Procedure

Out of 125 screened subjects, 95 patients provided written informed consent for enrollment. However, only 85 patients were followed-up for the six months, and the dropout rate was 10.5%. The recruited participants were randomized into two groups. Group one started with TI and crossed over to TII, and group two started with TII and crossed over to TI after the washout period (Figure 1)

Freshly roasted unsalted peanuts were packaged in separate bags of 80 grams each as the daily serving (variety: Red Valencia). Each package contained a thirty-day serving and provided to the participants to carry home and consume every day for four weeks after which they would refer for another batch for the following four weeks. The peanuts were consumed as part of the participants' snack or with their main meals.

Dietary intake was obtained by a 24-hour recall from 20% of the samples.

Fasting blood samples were collected at 7.00-8.00 AM. Approximately five milliliters of venous blood was collected to measure the fasting lipid profile, transferred to heparinized tubes, and centrifuged at 3,000 grams for three minutes. Serum and plasma were separated using an automatic pipette and transferred into specific labeled tubes in a rack for analysis. Lipid profile assays were routinely analyzed on the Mindray BS series autoanalyzer (Mindray-Bio Medical GmbH, Hamburg, and Germany) using established techniques.

Ethical clearance was sought from Kenyatta University Ethical Review Committee (REF:KU.R/COMM/51/273), the required permit was obtained from NACOSTI (REF: NCST/RCD/12A/013/4), and informed consent was obtained from the participants.

Statistical Analysis

Data analysis was performed in MS Excel spread sheet, and the analyzed data were exported to SPSS version 20 for analysis. Student's t-test was used to assess the significant difference in the lipid profile of the two treatment arms from baseline. In all the tests, the level of significance was set at P<0.05. In addition, data analysis for the 24-hour dietary recall was focused on the total energy and fat intake, saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs), protein, carbohydrate, vitamin E, folate, magnesium, and dietary fiber.

Nutrient composition was analyzed using the Nutrition Survey (2014) program, and one-way analysis of variance (ANOVA) was used to compare nutrient intake between the three random 24-hour recalls. In addition, Chi-square was applied for categorical variables such as the socio-demographic data, and paired student's t-test was used to compare the differences of the subjects in terms of various outcomes at baseline and the end of each treatment period. The Framingham risk score was also calculated for each individual based on variables such as age, gender, smoking habits, diabetes status, systolic blood pressure, total cholesterol, and high-density lipoprotein (HDL)-cholesterol. The Framingham score was derived using the approximated 10-year added risk of CVD and classified as low (<10%), medium (10-20%), high (20-30%), and very high (>30%). [13]

Table 1. Baseline socio economic and demographic characteristics

	Category	Period of treatment N=85		P value χ
		GROUP1 (TI- TII) **n=45**	**GROUP2 (TII- TI)** **n=40**	
Age	18-29	0(0.0)	1(1.2)	0.592
	30-39	8(9.4)	10(11.8)	
	40-49	23(27.1)	18(21.2)	
	>50	14(16.5)	11(12.9)	
Sex	Male	10(11.8)	8(9.4)	0.802
	Female	35(41.2)	32(37.6)	
Marital status	Single parent	12(14.1)	10(11.8)	0.405
	Married/Living together	19(22.4)	14(16.5)	
	Divorced/Separated	7(8.2)	10(11.8)	
	Widowed	7(8.2)	4(4.7)	
	Single	0(0.0)	2(2.4)	
Level of education	Lower primary	3(3.5)	2(2.4)	0.892
	Upper primary	13(15.3)	15(17.6)	
	Secondary	22(25.9)	19(22.4)	
	College	3(3.5)	2(2.4)	
	University	1(1.2)	0(0.0)	
	No formal education	2(2.4)	2(2.4)	
Occupation	Agricultural labor	12(11.1)	15(17.6	0.515
	Employed(Salaried)	7(8.2)	7(8.2)	
	Merchant/ Trader	18(21.2)	11(12.9)	
	Housewife	3(3.5)	2(2.5)	
	Waged labor	5(5.9)	5(5.9)	

Results

The obtained results only apply to the participants who completed the two treatments. Group one included 48 participants, and group two included 47 participants. Three participants dropped out of the study before the completion of the first treatment. In group two, seven participants dropped out of the study, and three participants dropped out before the completion of treatment II since they could not attend the clinic monthly. In addition, three participants dropped out after the first treatment, and one patient died. Group one started with TI and crossed over to TII, while group two started with TII and crossed over to TI after the washout period. The baseline socioeconomic and demographic characteristics of the subjects were analyzed, and no significant differences were observed between the participants in the two treatment arms at baseline.

Table 2. Mean daily energy and nutrient intakes from three random-day 24-h recall

	Baseline	T1	T2
Energy (kcal/day)	1937.10±309.98 [a]	2056.02±224.12[a]	2091.99±307.47[a]
Fat (%energy)	21.82±6.22[a]	32.05±7.64[b]	32.76±6.91 [b]
SFA	14.61±9.33[a]	19.39±4.51 [a]	19.39±5.72 [a]
MUFA	16.33±7.95[a]	32.53±6.17 [b]	33.19±5.84[b]
PUFA	8.89±3.61 [a]	17.86±2.66 [b]	19.16±2.96 [b]
Cholesterol (mg)	118.91±157.18[a]	118.12±211.06[a]	103.34±206.23 [a]
Protein(% energy)	12.23±2.56[a]	13.88±3.19[a]	13.35±2.47 [a]
Carbohydrate (% energy)	66.00±7.77[a]	54.23±9.71 [b]	53.64±7.58[b]
Vitamin E	3.25±2.70[a]	8.87±2.13 [b]	8.80±1.48[b]
Folate (mg/day)	313.89±188.11[a]	387.40±229.22 [a]	395.12±230.52 [a]
Magnesium (mg/day)	489.68±102.89[a]	592.53±142.34 [a]	618.22±248.03 [a]
Carotene	456.32±1103.60[a]	2149.58±4765.67 [a]	1892.89±4173.92 [a]
Dietary fibre (g/day)	24.61±8.76[a]	29.57±10.78 [a]	31.87±9.11 [a]

Values presented as the mean±/standard deviation; n=17. Means with different superscript letters are statistically significant at (P< 0.05). ONE WAY ANOVA. PUFA- poly unsaturated fatty acid, MUFA- mono unsaturated fatty acids, SFA – saturated fatty acid. TI- Treatment I TII- Treatment II

Dietary intake

The baseline comparison of the estimated nutrient and energy intake between the study

groups indicated no significant differences in this regard. ANOVA was also used to compare the nutrient intake of the three random 24-hour recalls between the two groups. The 24-hour dietary recall was administered to 20% of the participants at three random times. Table 2 shows the mean change in the dietary intake after the addition of peanuts to the regular diet of the subjects (TI) and after the provision of counseling in the healthy diet plus 80 grams of peanuts (TII). The obtained results indicated a significant difference in fat intake between the baseline and the two treatments ($F_{[2, 48]}=13.185$; $P<0.05$). Similar findings were observed for carbohydrate intake ($F_{[2, 48]}=11.664$; $P<0.05$), PUFA intake ($F_{[2, 48]}=55.091$; $P<0.05$), vitamin E intake ($F_{[2, 48]}=37.614$; $P<0.05$) and MUFA intake ($F_{[2, 48]}=34.328$; $P<0.05$).

Compared to baseline, energy intake from fats significantly increased in the TI and TII groups ($P< 0.05$). Furthermore, MUFA and PUFA intake increased significantly during TI and TII ($P<0.05$), while no significant change was observed in the SFA intake. A significant decrease was also observed in carbohydrate intake during TI and TII ($P<0.05$). On the other hand, the dietary intake of vitamin E ($P<0.05$) increased significantly compared to baseline in both treatments ($P<0.001$). These changes could be attributed to addition of peanuts to the diet of the subjects. Notably, folate and magnesium did not change significantly in the two treatments compared to baseline, and no significant difference was observed between the dietary intakes of the two treatment.
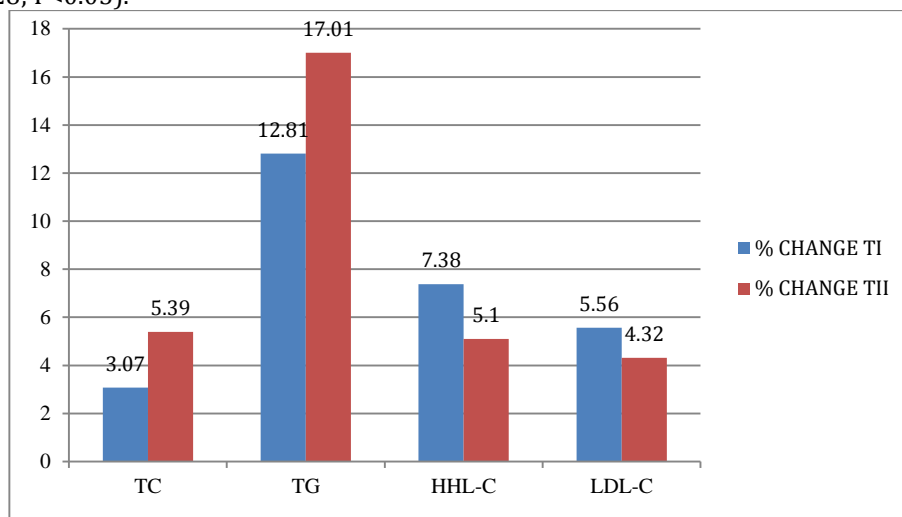

Figure 2. Percentage change in lipid profile in the two treatments Changes in Framingham's risk scores

C Changes in the Lipid Profile

Figure 2 shows the percentages of the changes in total serum cholesterol, serum TG, HDL-C, and low-density lipoprotein-cholesterol (LDL-C). A 3.07% decrease was observed in the total cholesterol of TI, while the reduction rate in TII was estimated at 5.39%. The reduction was considered significant in both treatments ($P<0.001$), and the mean change of the two treatments was also significant ($P<0.001$) (Table 3).

According to the findings, TG decreased in TI (12.81%), and the rate was estimated at 17.01% in TII. However, the mean change in the two treatments was not considered significant

($P=0.121$). A slight, significant increase was denoted in HDL-C in TI and II (7.38% and 5.1%, respectively) (Figure 1), and the mean change was considered significant in the two treatments ($P=0.012$) (Table 3).

In the present study, LDL-C reduced by 5.56% in TI and 4.32% in TII, and the change in this regard was significant in both treatments ($P<0.001$). However, the mean change in the two treatments was not considered significant ($P=0.242$). The mean reduction in the total cholesterol was more significant in the subjects with the total cholesterol of >5.1 mmol/l compared to those with the total cholesterol of <5.1 mmol/l.

Table 3. Mean change in serum lipid profile

	Treatment I				Treatment II				D1 &D2
	Baseline	End	D1	P value(t-test)	Baseline	end	D2	P value (t-test)	P value(t-test)
TC (mmol/L)	5.17±1.18	5.01±1.07	-.1589±.38	0.001	5.17±1.13	4.89±1.08	-0.27±0.20	0.001	0.001
TG (mmol/L)	1.88±.85	1.64±.83	-.24±.24	0.001	1.89±.90	1.57±.94	-0.32±0.48	0.001	0.121
HDL- C (mmol/L)	1.40±.41	1.51±.42	.10±.11	0.001	1.42±.42	1.49±.42	-0.07±0.09	0.001	0.012
LDL-C (mmol/L)	3.31±1.01	3.12±.92	-.18±.28	0.001	3.25±1.00	3.11±.99	.-14±25	0001	0.242

Values presented as the mean±/standard deviation; n=85. Means are statistically significantly different at (P< 0.05). TC- total cholesterol, TG- triglycerides, HDL-C- high density lipoprotein cholesterol, LDL-C- Low density lipoprotein cholesterol, D1- delta change in treatment I, D2- delta change in treatment II. Independent t-test was used to analyze the difference between the means.

Table 4. Change in Framingham's risk scores

	Baseline			End			P value (baseline& end)
Framingham's risk	Male	Female	P value (chi)	male	female	P value (chi)	
<10%	9(10.6)	42(49.4)	0.08	11(12.9)	44(51.8)	.356	0.03
10-20%	7(8.2)	25(29.4)		5(5.9)	23(27.1)		
20-30%	2(2.4)	0(0.0)		2(2.4)	0(0.0)		
>30%	0(0.0)	0(0.0)		0(0.0)	0(0.0)		

Approximated 10-years added risk of cardiovascular disease: low (< 10%), medium (10-20%), high (20-30%), and very high (> 30%). [1]

According to the current research, the mean reduction in TG was more significant in the participants with the TG of >2.25 compared to those with the TG of <2.25. The mean reduction in LDL-C was more significant in the participants with the LDL-C of >4.2 mmol/l compared to those with the LDL-C of <4.2 mmol/l. The mean increase in HDL-C was more significant in the participants with normal HDL-C levels (1.03-1.55), while the lowest value was observed in the participants with high HDL-C levels (>1.55). Total cholesterol and HDL-C were significantly different between the two treatments (P<0.001 and P<0.012, respectively), indicating that nutrition counseling on healthy diets increased HDL-C and decreased total cholesterol. On the other hand, regression analysis showed no correlations between the changes in the lipid profile of the two treatments and the changes in the PUFA, MUFA, and SFA intake as predicted.

The Framingham risk score was used to determine the 10-year risk of developing a CAD. Table 4 shows the changes in the Framingham risk score between the baseline and end of the study. The majority of the participants (60% and 64.7%) were at a low 10-year risk of CADs (<10%) at baseline and the end of the study,

respectively. Meanwhile, 2.4% of the participants were at a moderate 10-year risk of CADs (20-30%). The male and female subjects had no significant difference in terms of the 10-year risk at baseline and the end of the study period (P>0.05). However, a significant reduction was observed in the 10-year risk of CADs between the baseline and end of the study (P=0.03).

Discussion

The present study aimed to investigate the impact of peanut consumption and nutrition counseling regarding healthy eating on the serum lipid profile in HIV-infected patients. Three random 24-hour recalls were used to assess the dietary intake of the participants. According to the obtained results, energy intake did not change significantly when the regular diet of the subjects was supplemented with 80 grams of peanuts (TI) and when the patients were counseled on a healthy diet (TII). This could be due to the significant reduction of the carbohydrate intake in both treatments and the increased fiber intake, which might have led to early satiety and a non-significant increase in energy intake. These findings are consistent with the study conducted by Alper CM et al. [14], which was a 30-week crossover study in which the

subjects were provided with 500±136 kilocalories worth of peanuts for an eight-week free feeding (FF) diet. In another research, Mckiernan F. et al. [15] reported no significant changes in energy intake within a four-week randomized clinical trial. Compared to the baseline, energy intake from fats increased significantly during TI and TII (P<0.05) in the present study, and the MUFA and PUFA intakes also increased significantly during TI and TII (P<0.05). On the other hand, the SFA intake remained unchanged. Similar findings have been reported by Alper CM et al., McKiernan F. et al., and Lokko et al. [14-16].

In the current research, a significant decrease was denoted in carbohydrate intake during TI and TII (P<0.05), which is in line with the study by Alper CM et al., [14] while inconsistent with the study by McKiernan F et al. [15], which indicated no reduction in carbohydrate sources when peanut was added to a regular diet. Dietary intakes of vitamin E (P<0.05) increased significantly from the baseline in both treatments in the present study (P<0.05).

Our findings indicated a significant reduction in the total serum cholesterol in both treatments (3% and 5.3%, respectively). In addition, the change in TG was considered significant in both treatments (12.8% and 17.1%, respectively). On the other hand, LDL-C decreased significantly in both treatments (5.5% and 4.3%, respectively). Epidemiological studies and clinical trials have demonstrated the benefits of nuts and peanut consumption on the CAD risk and the associated risk factors [17, 18]. Our findings in this regard are consistent with the study by Lokko P. et al. [16], which demonstrated a total cholesterol decrease of 7.2%, while a 20% decline was also reported in TG after adding 500 kcal/day of peanuts to the daily diet of the subjects for eight weeks.

A recent four-week study conducted by McKiernan F. et al. [15] on hyperlipidemic patients indicated a significant reduction in the total serum cholesterol, LDL-C, and TG after consuming 56 grams of unprocessed whole raw peanuts, roasted unsalted/salted peanuts, honey grazed roasted peanuts, or peanut butter daily. However, HDL-C concentrations increased significantly compared to the baseline. Recently, a pooled analysis of 1,284 observations has been proposed from 583 unique participants in 25 clinical studies conducted in seven different countries using different nuts, including peanuts.

[19] The results of the mentioned pool showed that the exerted cholesterol-lowering effects were dose-dependent. Furthermore, the analysis indicated that 67 grams of the average daily intake of nuts could lead to the mean estimated reduction of 5% in total cholesterol and 7% in LDL-C. However, nuts intake had no significant effects on HDL-C and TG, while the effects were reported to be significant on the participants with serum TG of >150 mg/dl (10.2 mg/dl reduction observed).

In the present study, the mean reduction in the total serum cholesterol, LDL, and TG was higher but not significantly higher in the participants with high serum levels compared to those with normal serum levels. This is inconsistent with an interventional study with peanuts, which demonstrated a reduction in total cholesterol (12%) and LDL-C (10%) in the normocholesterolaemic patients consuming whole peanuts and peanut butter for 24 days. [20] (Kris-Etherton et al., 1999).

The current research indicated no significant correlation between the changes in the dietary PUFA, MUFA, fat, and fiber individually or together and the changes in the lipid profile of the patients based on linear regression analysis. This is because there are other components in nuts (e.g., fiber and phytosterols) along with unsaturated fatty acids, which are likely to contribute to the favorable effects of nuts on the plasma lipid. [21-23]

In the present study, the reduction of TG may have resulted from the decreased carbohydrate intake of the subjects following the addition of peanuts to their diet. According to the literature, TG concentration decreases with reduced carbohydrate intake. [24] Therefore, the reduction of carbohydrate intake might have exerted an independent effect on the lipid profile of our participants. It is estimated that the reduction of total cholesterol and LDL-C by 1 mmol/l may result in a 24-28% decrease in the relative mortality risk of coronary heart disease. In addition, TG reduction by 1.0 mmol/l may result in a 14-37% decrease in the total risk of CVDs. [25] The present study had a crossover clinical trial design, which reduced interpersonal variations. However, it was performed on free living individuals under the assumption that the provided peanuts were consumed daily and not shared with other family members.

Conclusion

According to the results, the consumption of peanuts with and without counseling on a healthy diet could improve the lipid profile of the subjects living with HIV infection, thereby reducing the 10-year risk of developing coronary heart disease.

Acknowledgements

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