



Cardiovascular Diseases Risk Reduction And Lifestyle Modification: Cross Sectional Analysis Of Patient Responses.

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ABSTRACT

A decrease in cardiovascular event risk with a decrease in total and LDL – cholesterol level is termed as “cholesterol paradox” or “risk factor reversal”. Cardiovascular risk does not have a linear relationship between LDL – cholesterol levels, and other substantial risk factors of cardiovascular events are being disregarded. The aim of this study is, to identify modifiable risk factors of cardiovascular events other than those well proved to cause dyslipidemia. A cross-sectional study was conducted with 652 participants in a tertiary care hospital. Patients were grouped into two, based on the history of cardiovascular events. Demographics and patient responses captured using pre-validated questionnaires were analyzed. 5mL blood samples were collected by venipuncture and lipid profile was estimated. Association between cardiovascular events and explanatory variables. was determined using Chi square test and Odds ratio at 95% confidence intervals. Higher risk of CV events was found among smokers 0.232 [0.144 – 0.373]. Consumption of white sugar, refined oil, processed cold beverages and fast food products increased CV risk respectively. Moreover, total cholesterol, LDL-C and triglycerides were found to decrease after one year of counselling the patients. The classical hypothesis of dyslipidemia induced atherosclerosis may not be the predominant cause of CV events. Herein, we report no association between high fat diet and CV risk while we observed higher risk in consumers of refined and ultra processed food products. However, significant control of cholesterol was observed in patients who shifted to Unrefined food products.

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Keywords: Cardiovascular, hypercholesterolemia, refined food, ultraprocessed, atherosclerosis

1. INTRODUCTION

Most cardiovascular disorders are caused by atherosclerosis, which can result in rapid death from ischemic heart disease or ischemic stroke¹. Atherosclerosis, which is often asymptomatic, is linked to a poor prognosis, a high fatality rate, and a shorter life expectancy². Dyslipidaemias, notably increased plasma LDL - cholesterol (low density lipoprotein) levels and hypertriglyceridemia, are well recognised and accepted etiologies of atherosclerotic plaque deposition inside blood arteries^{3,4}. The findings that patients treated with HMG CoA reductase inhibitors, had a lower cardiovascular risk support the concept that dyslipidemias are the cause of atherosclerotic plaques⁵. Low cholesterol levels, on the other hand, have been linked to a higher risk of death in a few studies⁶⁻⁸. Despite a considerable drop in LDL cholesterol and a concurrent increase in HDL – cholesterol, cardiovascular risks in patients remain unchanged in evacetrapib (ACCELERATE) clinical trial results⁹. These contradictory findings show, that dyslipidemias may not be the main source of cardiovascular risk, and that other processes may be at work as well. Though numerous RCTs have shown statins to reduce cardiovascular risk, it is equally important to note the findings of several RCTs that have found no significant link between lower cholesterol levels and increased cardiovascular risk¹⁰⁻¹². Approximately 40 randomised controlled trials (RCTs) using cholesterol-lowering drugs such as statins, clofibrate, ezetimibe, and evacetrapib have found no reduction in mortality or cardiovascular events¹³. Furthermore, only a few RCTs¹⁴ have found a significant risk with cholesterol-lowering drugs. Based on the findings, we postulated that cardiovascular risk is not linearly related to LDL cholesterol levels, and that other significant risk factors for cardiovascular events are being overlooked. Consumption of ultra-processed and refined foods, for example, has been shown to have negative effects, on cardiovascular health via other processes such as the Maillard reaction¹⁵. Bishpenol A, carrageenan, emulsifiers, glutamates, and sulphites, which are included in ultra-processed and refined foods, have been shown to enhance cardiovascular risk in both people and animal models¹⁶. Obesity, hypertension, and dyslipidemia are more common in habitual consumers of refined food items, implying that dietary adjustments should be done by switching to Unrefined food products rather than applying dietary restrictions as a normal practise¹⁷. Furthermore, the so-called 'risk factor reversal' phenomenon of increased cardiovascular events with low total cholesterol and LDL-cholesterol, is attributed to a variety of plausible mechanisms, including adipokine protection against tumour necrosis factor – and inflammatory process modulation in obese and dyslipidemic patients¹⁸. The cholesterol paradox is thought to be caused by indirect processes, such as early medication beginning and unfavourable symptoms of comorbidities such as malnutrition and malabsorption¹⁹. As a result, we postulated that non-dyslipidemic modifiable cardiovascular risk factors exist. Hence this study was designed to determine non-dyslipidemic modifiable cardiovascular risk factors and compare the risk of cardiovascular events between patients who consume refined and non-refined products.

2. METHODOLOGY

In December 2020, the global prevalence of cardiovascular disorders is approximately 15 percent, considering which yielded a sample size of minimum 652 study participants²⁰. Stratification was executed on all patients based on the prior history of cardiovascular events including acute coronary syndromes. The selection consisted of 568 patients, without prior history of cardiovascular patients and 84 patients with a prior history of cardiovascular events. The following inclusion criteria were considered during subject recruitment: (a) Adult patients of age between 18 years and above, either gender; (b) Patients with or without a prior history of cardiovascular events; (c) Patients who are willing to provide a written informed consent. Patients meeting either of the following criteria were excluded participation: (a) Patients with a clinical diagnosis of any psychiatric illness, including but not limited to schizophrenia, bipolar disorder, major depression and anxiety disorders; (b) Patients diagnosed with cognitive and neurodegenerative disorders, including Alzheimer's disease, age related dementia, Parkinsonism, multiple sclerosis, amyotrophic lateral sclerosis and malignancies with CNS invasion; (c) Pregnant women. A pre-validated food preferences and frequency questionnaire, including 3 domains and 15 items was given to the subjects. For each question in food frequency, the following categories of consumption frequency were possible: I never eat/ consume very rare, rare, frequent, and very frequent. Food preferences and type of food preferences were not quantitative and were measured in nominal scale. The validity of the food frequency questionnaire was tested on 10% of the estimated sample size i.e. 65 patients. Among the 568 patients without prior history of cardiovascular risk, 106 patients volunteered to provide a 5mL blood sample without any incentive. The 106 patients were again sub-stratified based on the type of food products they frequently use: refined or Unrefined. Blood was collected by venipuncture from median cubital or cephalic veins. Samples were collected in plasma separator vacutainer and transferred to laboratory for estimation of lipid profile. Baseline lipid parameters were estimated in both the groups and

compared. A clinically and linguistically validated set of information in the form of powerpoint presentation was used as intervention to counsel patients on the health benefits of Unrefined food products. Patients who were on refined and ultra-food products were encouraged to consume unrefined food products for a period of 12 months from the date of intervention. Patients were followed up after 12 months and lipid parameters were estimated. Lipid parameters were compared before and after the intervention to find out the effect of unrefined food products on blood cholesterol level. For descriptive statistics, frequencies were calculated for individual characteristics versus risk factors. Individual characteristics were age, gender, Body Mass Index (BMI) classified according to the World Health Organization underweight, healthy, overweight and obese. Literacy level (Illiterate, primary school, high school and university); marital status (unmarried, married and prefer not to say); diet (vegetarian and mixed); smoking (yes/no) and alcoholism (yes/no). Two sided tests at 95% confidence level were used depending on data normality. For comparison on baseline population means of lipid levels between patients on refined and Unrefined food products, unpaired t test was used. Paired t test was used for comparison of sample means of lipid levels before and after the intervention. All statistical analyses were performed using R Studio 4.0. Bar and cluster graphs were constructed using Microsoft Excel. The institutional ethics committee of Agarwal's Eye Hospital approved the study protocol All patients enrolled provided written informed consent for participation (ECR/921/Inst/TN/2017/RR-20)..

3. RESULTS

A total 652 patients were provided with the questionnaire and responses were collected in the data capture form. Patient recruitment process was carried out as shown in **Fig 1**. Among the 652 enrolled participants 84 (12.9%) patients had a prior history of cardiovascular event while 568 (87.1%) patients did not have any prior history of cardiovascular event.

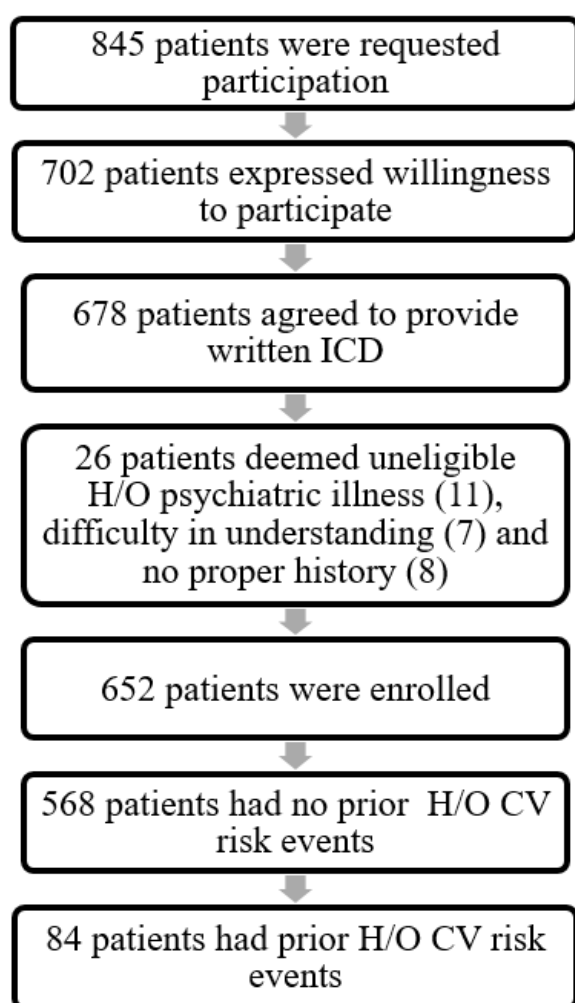


Fig 1: Patient Recruitment Process

S. No.	Parameter	Study Group		Odds Ratio	P Value	
		Without CV event (n=568)	With CV event (n=84)			
1.	Age (years)	49.3 ± 14.6	51.8 ± 12.4	-	0.186	
2.	Gender	Male	277	62	0.338 [0.202 – 0.564]	0.000**
		Female	291	22		
3.	BMI	Underweight	81	14	0.832 [0.448 – 1.546]	0.619
		Healthy	262	42	0.856 [0.541 – 1.354]	0.558
		Overweight	133	16	1.299 [0.729 – 2.317]	0.407
		Obese	92	12	1.160 [0.605 – 2.223]	0.750
4.	Literacy level	Illiterate	122	21	0.820 [0.482 – 1.398]	0.481
		Primary School	147	18	1.280 [0.736 – 2.228]	0.422
		High School	164	20	1.299 [0.762 – 2.216]	0.366
		University	135	25	0.736 [0.444 – 1.221]	0.276
5.	Marital status	Unmarried	121	11	1.859 [0.956 – 3.616]	0.0819
		Married	432	73		
		Prefer not to say	15	4	-	-
6.	Diet	Vegetarian	51	12	0.591 [0.301 – 1.163]	0.163
		Mixed	517	72		
7.	Smoking	Smoker	111	43	0.232 [0.144 – 0.373]	0.191
		Non-smoker	457	41		
8.	Alcoholism	Alcoholic	155	28	0.751 [0.460 – 1.225]	0.245
		Non-alcoholic	413	56		

The mean age of the overall study population was found to be 45.9 ± 15.2 years. Summary of demographics of the study participants is shown in **Table 1**. Statistically significant differences were not observed in demographic parameters other than gender. Thus the baseline features matched between patients with and without cardiovascular events. It is crucial to note that the risk of cardiovascular events did not significantly differ between vegetarians and mixed diet consumers. One hundred and six patients volunteered to provide blood samples. Among them 77 patients consumed refined food products and 29 patients consumed Unrefined food products.

S. No.	Comorbidities	Frequency	
		Without CV event (n=568)	With CV event (n=84)
1.	Diabetes Mellitus	235	58
2.	Hypertension	216	73
3.	Bronchial Asthma	147	12
4.	COPD	70	6
5.	Epilepsy	48	2
6.	Malignancy	21	0
7.	Pulmonary tuberculosis	36	3
6.	Hypothyroidism	91	12
7.	Hyperthyroidism	10	0

8.	Chronic kidney disease	38	2
9.	Diabetic retinopathy	22	13
10.	Myocardial infarction	-	53
11.	Stroke – Ischemic	-	31
12.	Stroke – Hemorrhagic	2	0
13.	Deep vein thrombosis	-	18
14.	Varicose veins	53	10
15.	Infectious diseases (excluding PTB)	131	28
16.	Cardiac arrhythmias	27	8
17.	Osteoarthritis	20	1
18.	Rheumatoid arthritis	6	0
19.	Glaucoma	179	11
20.	Cataract	208	29
21.	Others	69	4

In the overall study population 44.9% patients had diabetes mellitus, 44.3% patients had hypertension , 36.3% patients had cataract, 29.1% patients had glaucoma while 24.4% patients had bronchial asthma and infectious disease other pulmonary tuberculosis respectively. Among the diseases that occurred with relatively less frequency 15.8% patients had hypothyroidism, 11.7% had COPD, 9.7% had varicose veins, 8.1% had myocardial infarction, 7.7% had epilepsy, 6.1% had chronic kidney disease, 6.0% had pulmonary tuberculosis 5.4% had diabetic retinopathy, 5.4% had cardiac arrhythmia, 3.2% had malignant tumours and osteoarthritis respectively.

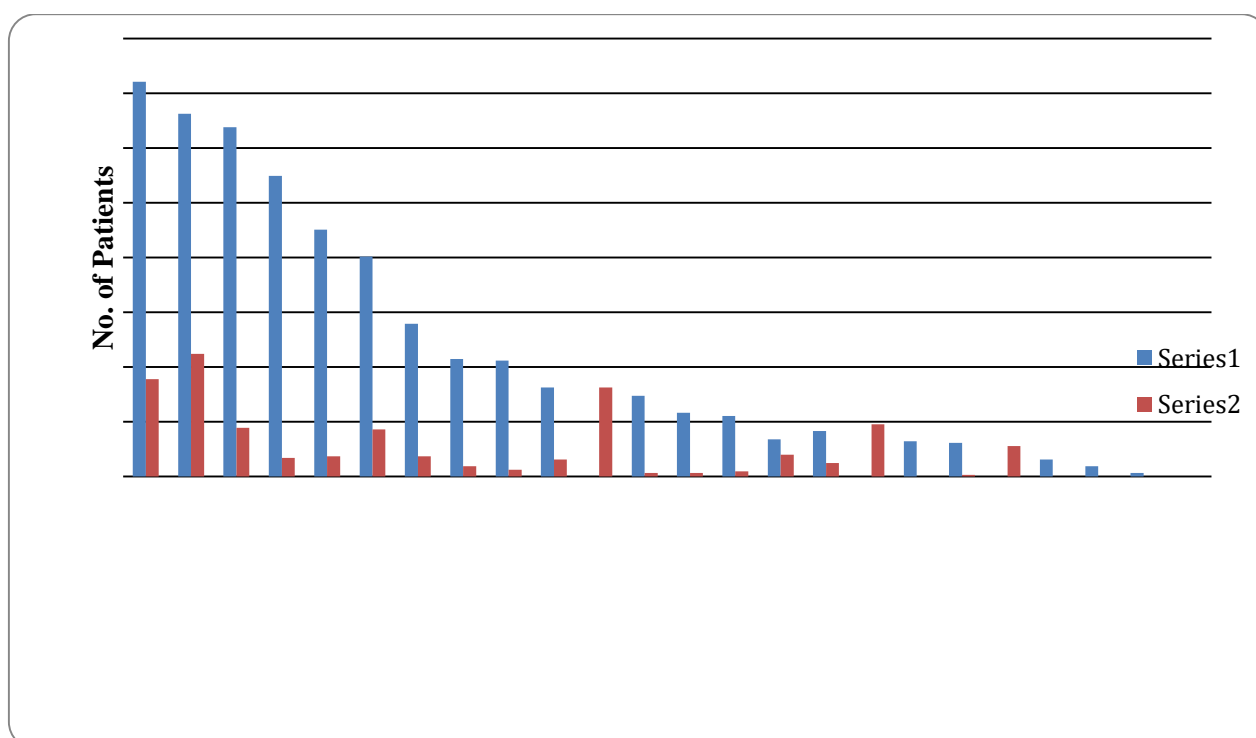
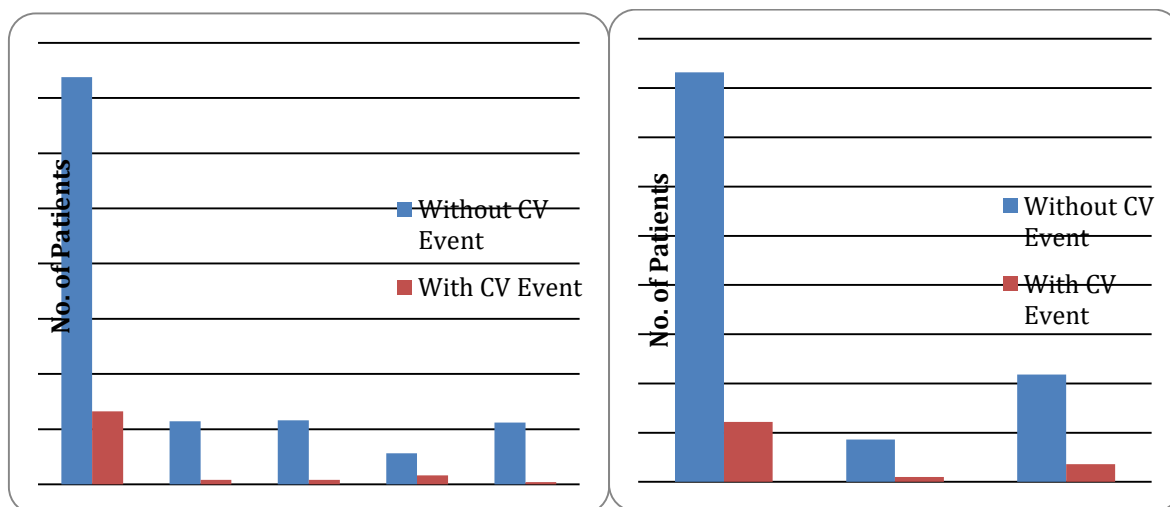


Fig 2: Comparison of comorbidities between patients with and without cardiovascular risk. Series 1: Patients with CV events; Series 2: Patients without CV events.

S. No.	Item	Response		Odds Ratio	P Value
		Without CV event (n=568)	With CV event (n=84)		
1.	Type of White sugar	369	66	1.976 [1.142-3.425]	0.013*

		Brown sugar	57	4	0.448 [0.158- 0.159 1.269]
		Honey	58	4	0.440 [0.155- 0.160 1.244]
		Sugar free	28	8	1.026 [0.572- 0.882 1.838]
		Others	56	2	0.223 [0.053- 0.022* 0.932]
2.	Type of milk	Cow milk	416	61	0.969 [0.579- 0.896 1.621]
		Powdered milk	43	5	0.773 [0.297- 0.822 2.008]
		Other	109	18	1.148 [0.655- 0.658 2.012]
3.	Type of oil	Refined oil	248	71	7.042 [3.817- 0.000**** 12.987]
		Non - refined oil	320	13	
4.	Type of food	Curry/ Gravy	209	27	0.814 [0.499- 0.466 1.333]
		Fried	74	14	1.335 [0.715- 0.392 2.494]
		Both	247	35	0.929 [0.583- 0.814 1.477]
		Others	38	8	1.468 [0.660- 0.359 3.268]

* *P*-value significant at 95% CI.



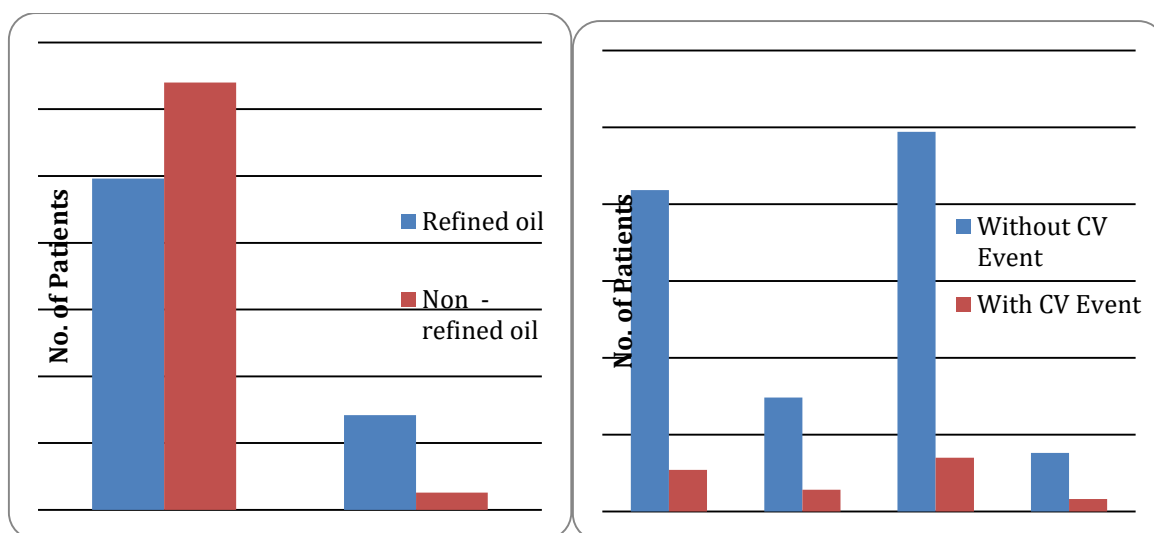


Fig 3: Dietary Practices at Home between Patients with Cardiovascular Event and without Cardiovascular Event

A 97% increased risk of CV events was observed in patients who regularly consumed refined white sugar than those who consumed brown sugar or honey at a level of significance of 0.05. While consumption of refined sugar products increases CV risk on the other hand a minor increase in cardiovascular risk is also observed in patients who prefer a sugar free diet though statistically inconsistent. Statistically significant association was not observed between type of milk consumed and cardiovascular risk. A 7-fold increased risk of cardiovascular events was observed in patients who regularly consumed refined oil products at a level of significance of 0.01. Type of cooking food such as curry or fried did not have any statistically significant association with cardiovascular risk. The risk of cardiovascular events occurring was compared between patients who are frequent consumers and relatively

less frequent consumers and the results are summarized in **Table 4**.

Table 4: Comparison of Frequency of Food Consumption between Patients with and without Cardiovascular Events													
S. No.	Item	Response										Odds Ratio	P Value
		Without CV event (n=568)					With CV event (n=84)						
		0	1	2	3	4	0	1	2	3	4		
1.	How often do you drink coffee/tea or other hot beverages?	38	25	16	358	131	8	6	1	49	22	0.765	0.409
												[0.417 – 1.401]	
2.	How often do you drink soft drinks/packed fruit drinks or other cold beverages?	85	199	142	85	57	17	24	18	15	10	1.271	0.038*
												[1.167 – 2.106]	
3.	How often do you eat fast food from a restaurant?	80	148	185	103	52	6	14	10	33	21	4.796	0.000****
												[2.959 – 7.775]	
4.	How often do you consume fish, eggs or other red meat?	52	28	45	352	91	8	4	7	52	13	0.965	0.889
												[0.558 – 1.671]	
5.	How often do you eat vegetables?	0	8	3	504	53	0	2	5	56	21	0.217	0.005**
												[0.082 – 0.577]	

6.	How often do you consume sweets?	113	27	153	171	104	17	4	23	25	15	0.969	0.907
												[0.612 –	
												1.533]	

0 = I never eat/ consume, 1 = Very rare, 2 = Rare, 3 = Frequent, 4 = Very Frequent.

Patients who responded as 'I never eat or consume' or 'very rare' or 'rare' were grouped together as less frequent consumers while patients who responded as 'frequent' or 'very frequent' were grouped together as frequent consumers. Higher consumption of coffee/ tea or other hot beverages was not found to be associated with cardiovascular risk but 27.1% increased cardiovascular risk was observed in patients who are frequent consumers of processed and stored cold beverages. Similarly a 4-fold increased CV risk was observed in patients who frequently consumed from fast food restaurants. Higher consumption of fish, egg or other red meat was not found to increase CV risk while patients with higher consumption of vegetables had 21.7% decreased CV risk. No significant association between frequency of sweet intake and CV risk was observed. Differences in baseline lipid parameters between patients on refined and unrefined food products are shown in **Table 5**.

Table 5: Comparison of Baseline Lipid Profile between Patients on Refined and Unrefined Food Products

Parameters	Group I (n=77)		Group II (n=29)		P Value
	Mean ± SD	Median	Mean ± SD	Median	
Total Cholesterol	203.9 ± 18.5	204	186.2 ± 3.474	184	<0.0001*
LDL	124.4 ± 14.9	125	119.6 ± 3.025	117	< 0.0001*
VLDL	34.1 ± 4.2	34	34.90 ± 1.647	37	0.2264
HDL	44.2 ± 10.1	46	31.71 ± 1.882	30	0.2583
Triglycerides	194.6 ± 11.22	196	176.7 ± 21.8	178	0.0012*

Group I: Patients on refined food products, Group II: Patients on Unrefined food products; Confidence level: 95%; Level of significance: 0.05. Baseline lipid parameters of 106 patients without prior CV events were estimated and comparison was made, between the lipid parameters of patients on refined and unrefined food products. Statistically significant differences were observed between the population means of total cholesterol, LDL and triglycerides with a mean difference of 17.7 ± 15.0 mg/dL, 4.8 ± 11.9 mg/dL and 17.9 ± 10.58 mg/dL respectively. It is evident from the observations that TC, LDL-C, VLDL, HDL and triglycerides are under control in patients who consume Unrefined food products. Differences in lipid parameters before and after patient counselling are shown in **Table 6**.

Table 6: Comparison of Lipid Profile before and after Patient Counselling in Group I Patients

Parameters	Before (n=77)		After (n=61)		P Value
	Mean ± SD	Median	Mean ± SD	Median	
Total Cholesterol	203.9 ± 18.5	204	189.9 ± 17.6	190	<0.0001*
LDL	124.4 ± 14.9	125	108.1 ± 12.9	109	< 0.0001*
VLDL	34.1 ± 4.2	34	31.6 ± 3.9	32	0.0008
HDL	44.2 ± 10.1	46	50.2 ± 11.5	52	0.0026
Triglycerides	194.6 ± 11.22	178	157.8 ± 19.5	159	< 0.0001*

Clinically significant improvement in lipid parameters was observed after 12 months of Unrefined food products consumption. Statistically significant differences in sample means of total cholesterol, LDL-cholesterol and triglycerides were observed between before and after the intervention. A mean decrease of 14 ± 0.9 mg/dL, 16.3 ± 2.0 mg/dL and 36.8 ± 8.3 mg/dL was observed for total cholesterol, LDL-cholesterol and triglycerides respectively after 12 months of consumption of Unrefined food products. These findings suggest that Unrefined food products favour better control of cholesterol and lipids in patients with dyslipidemia and can therefore decrease the risk of cardiovascular events. Comparison of lipid parameters before and after the intervention is shown graphically in **Figures below**.

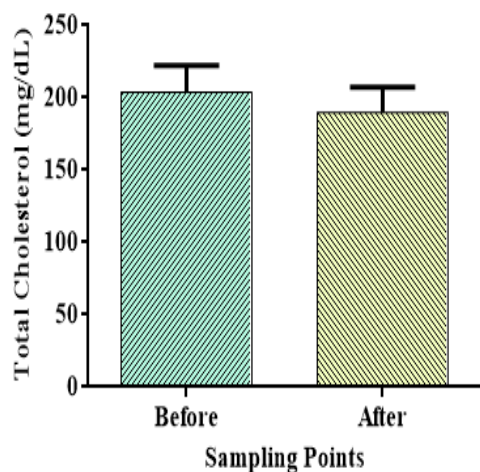


Fig 2: Comparison of total cholesterol before and after intervention

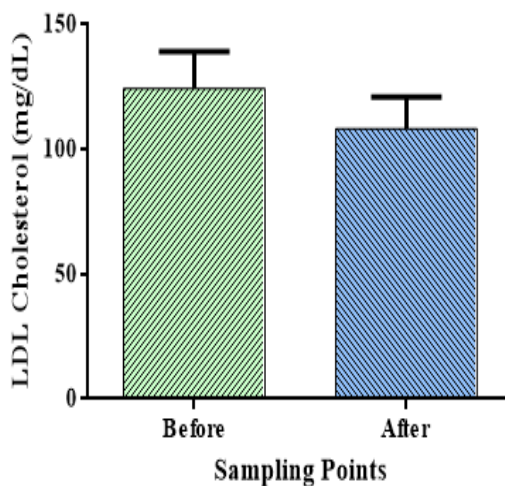


Fig 3: Comparison of LDL before and after intervention

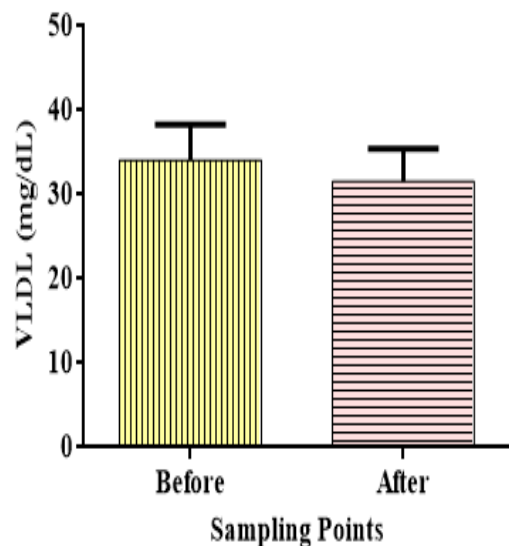


Fig 4: Comparison of VLDL cholesterol before and after intervention

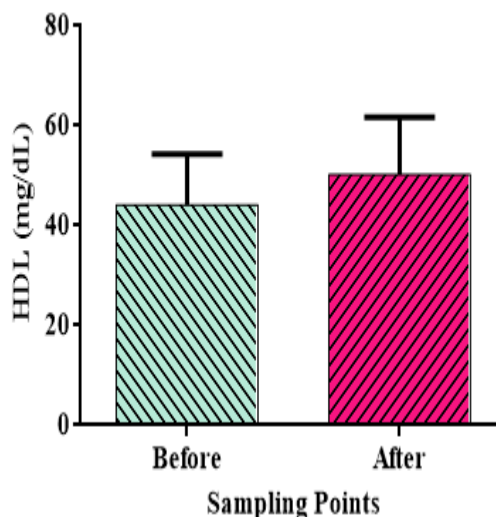


Fig 5: Comparison of HDL cholesterol before and after intervention

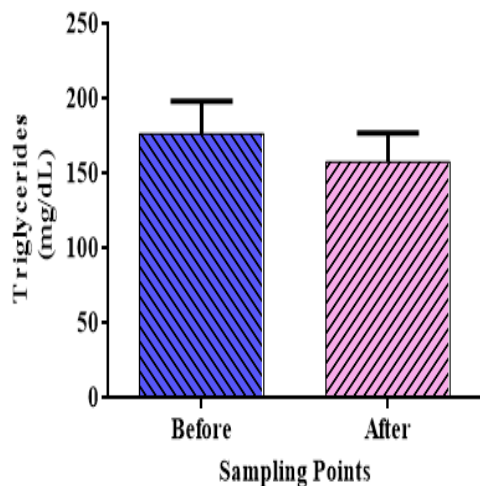


Fig 6: Comparison of triglycerides before and after intervention

4. DISCUSSION

A decrease in cardiovascular event risk with a decrease in total and LDL – cholesterol level is termed as “cholesterol paradox” or “risk factor reversal”²¹. Though the well proved theory of hyperlipidemia causing atherosclerosis cannot be completely rebutted, it is pivotal to contemplate the major risk posed by non-dyslipidemic causes of cardiovascular events. Majority of these risk factors are modifiable, and are predominantly associated with dietary habits²². In our study, demographic characteristics did not significantly differ between the patients with and without cardiovascular risk except gender. The decreased risk of CV events in male patients observed in our study could be due to the fact that female patients are naturally protected from CV events by estrogen hormones^{23,24}. It is crucial to note that significant differences in CV risk was not observed due to dietary preferences (i.e. Vegetarian or Mixed). A meta-analysis of eight observational studies reported, that vegan diet was associated with decreased risk of cardiovascular mortality (RR: 0.70 [0.55–0.89], 95% CI) while all cause mortality remained the same (RR: 0.84 [0.65–1.07], 95% CI)²⁵. Herein, we observed higher CV risk in smokers than non-smokers. While polycyclic aromatic hydrocarbons produced by cigarette smoking up regulate the transcription of genes involved in inflammatory pathways, tetrachlorodibenzodioxin has been shown to accelerate the atherosclerotic process in invivomodels²⁶. We analyzed the dietary preferences of patients with cardiovascular events and compared patients without cardiovascular events. Though dietary preferences did not significantly alter the risk of cardiac events, a significantly lower cardiac risk was observed in patients who consume Unrefined food products. For instance, consumption of refined white sugar had higher odds of developing CV events as seen with consumption of refined oil. The higher risk could be attributed to the presence of chemical contaminants used, while refining and ultra-processing of food products²⁷. In addition, refined oils are rich in polyunsaturated fatty acids, which upon degradation produce highly atherogenic and mutagenic substances including free radicals, trans fats and malondialdehyde [26]. Moreover, exposure to intense physical and chemical processes of extraction, led to loss of antioxidants such as tocopherol and produce atherogenic polymeric components²⁸. We examined the frequency of specific food item consumption, and observed that regular consumption of meat, egg and fish products did not alter CV risk. However, an increase in CV risk was observed in patients who regularly consumed processed & packed beverages. An observational study by Pacheco LS has reported that consumption of more than one serving per day of sugar sweetened beverages increases the risk of cardiovascular disorders (CVD), revascularization and stroke (HR, 1.19; 95% CI, 1.06–1.34)²⁹. It is thus evident that processed and sugar sweetened beverages are a modifiable risk factor of CVD. Frequent consumers of fish, egg and red meat did not have increased cardiovascular risk in our study. Red meat is high in cholesterol as well as saturated and unsaturated fatty acids. One of the risk factors for metabolic diseases is its consumption. A number of studies have found a link between red meat consumption and cardiovascular disease (CVD). Although a prospective cohort study on the US adult population has shown 15% increased risk of coronary artery disease among red meat consumers (HR, 1.15; 95% CI, 1.06 to 1.25), whole grains and dairy products in place of total red meat, and eggs in place of processed red meat, were linked to a decreased risk of coronary artery disease (HR, 0.86; 95% CI, 0.80 to 0.93)³⁰. However a meta-analysis of 47 observational studies has indicated that a higher fish intake in the diet is linked to a lower risk of CHD and mortality³¹. The following is a plausible explanation for decreasing CVD with fish intake. Because of its anti-arrhythmic and anti-inflammatory effects, as well as its ability to alleviate endothelial dysfunction, N-3 long chain polyunsaturated fatty acids present in fish meat may play a significant part in this process. Seafood-derived N-3 long chain polyunsaturated fatty acids can have electrophysiological benefits after being integrated into cell membrane phospholipids, such as improved cardiac ion channel activity and cell signalling pathways, as well as increased cell membrane fluidity. These effects have been associated with a lower risk of ventricular arrhythmias and sudden death in the heart³². Higher consumption of vegetables was found to decrease CV risk in our study. A systematic review and dose-response meta-analysis of prospective studies has linked consumption of fruits and vegetables to a lower risk of cardiovascular events, malignancies, and all-cause mortality (RR, 0.92; 95% CI, 0.90–0.94). Lowest risk of coronary artery disease, stroke, and all-cause mortality was observed at 800 g/day (10 servings/day) of fruit and vegetable intake, a quantity that is double the quantity (400 g/day) currently recommended by the World Health organization (WHO)³³. Patients without prior history of cardiovascular events and who volunteered to provide blood samples and return for follow up after 12 months were alone stratified into two groups based on whether they frequently used refined or unrefined food products. Shift to Unrefined food products from refined food products was hypothesized as intervention. A systematic review and network meta-analysis to compare cardiovascular benefits of refined oils with non-refined oils reported that unsaturated fatty rich oils like safflower, sunflower, rapeseed, flaxseed, corn, olive, soybean, palm, and coconut oil were more effective in reducing LDL-C as compared with saturated fatty acid rich food like butter

or lard³⁴. Herein we observed a statistically significant difference in baseline lipid parameters between patients who are frequent consumers of refined and unrefined food products. Moreover, significant decreases in total cholesterol, LDL-cholesterol and triglycerides were observed after 12 months of switching to a diet rich in unrefined food products. This can be attributed to the fact that refined grains and added sugars, salt, trans fats, and animal-source foods are abundant in poor-quality diets, whereas whole grains, fruits, vegetables, legumes, fish, and nuts are scarce. They are frequently rich in processed food products, which are typically packed and precooked, and low in whole foods and freshly made dishes³⁵. Systematic reviews and high-quality RCTs back up the idea that highly refined, high-glycemic-load carbs are hazardous. A large Danish prospective cohort study on the effects of swapping saturated fats with high-GI carbs discovered that substituting saturated fat with high-GI carbohydrates raises the incidence of myocardial infarction (MI) by 33%^{36,37}. Polished white rice, starch, and white wheat flour are examples of highly refined carbohydrates with low fibre content³⁸. Higher refined grain intake was linked to higher waist size, systolic and diastolic blood pressure (SBP and DBP), fasting glucose, triglycerides, and insulin sensitivity, as well as lower HDL-C values in the cross-sectional CURES 57 trial³⁹. Thus it is evident that switching to unrefined food products is effective in achieving better lipid control and hence unrefined food products should be promoted for decreasing cardiovascular events in high risk populations.

5. CONCLUSION

The classical hypothesis of dyslipidemia induced atherosclerosis may not be the predominant cause of CV events. Herein we report no association between high fat diet and CV risk while we observed higher risk in consumers of refined and ultra-processed food products. Cardiometabolic disorders such as obesity, hypertension and dyslipidemia occur at higher incidences in regular consumers of refined food products suggesting that dietary changes should be made by shifting to unrefined food products rather than implementing the routine practice of dietary restrictions.

AUTHOR CONTRIBUTION STATEMENT

Mrs Sumathy T and Maheshkumar V P conceptualized and gathered the data with regard to this work. Maheshkumar V P and Jaikumar S analyzed these data and necessary inputs were given towards the designing of the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

REFERENCES

1. Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, Tokgözoğlu L, Lewis EF. Atherosclerosis. *Nat Rev Dis Primers*. 2019 Aug 16;5(1):56. Doi: 10.1038/S41572-019-0106-Z. PMID: 31420554.
2. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology Of Coronary Heart Disease And Acute Coronary Syndrome. *Ann Transl Med*. 2016;4(13):256. Doi:10.21037/Atm.2016.06.3.
3. Ference BA, Ginsberg HN, Graham I, Et Al. Low-Density Lipoproteins Cause Atherosclerotic Cardiovascular Disease. 1. Evidence From Genetic, Epidemiologic, And Clinical Studies. A Consensus Statement From The European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459-2472. Doi:10.1093/Eurheartj/Ehx144.
4. Peng J, Luo F, Ruan G, Peng R, Li X. Hypertriglyceridemia And Atherosclerosis. *Lipids Health Dis*. 2017 Dec 6;16(1):233. Doi: 10.1186/S12944-017-0625-0.
5. Byrne P, Cullinan J, Smith A, Smith SM. Statins For The Primary Prevention Of Cardiovascular Disease: An Overview Of Systematic Reviews. *BMJ Open*. 2019;9(4):E023085. Published 2019 Apr 23. Doi:10.1136/Bmjopen-2018-023085.
6. Bae JM, Yang YJ, Li ZM, Ahn YO. Low Cholesterol Is Associated With Mortality From Cardiovascular Diseases: A Dynamic Cohort Study In Korean Adults. *J Korean Med Sci*. 2012;27(1):58-63. Doi:10.3346/Jkms.2012.27.1.58.
7. Nago N, Ishikawa S, Goto T, Kayaba K. Low Cholesterol Is Associated With Mortality From Stroke, Heart Disease, And Cancer: ThejichiMedical School Cohort Study. *J Epidemiol*. 2011;21(1):67-74. Doi:10.2188/Jea.Je20100065.
8. Simes RJ. Low Cholesterol And Risk Of Non-Coronary Mortality. *Aust N Z J Med*. 1994 Feb;24(1):113-9. Doi: 10.1111/J.1445-5994.1994.Tb04446.X.

9. Filippatos TD, Elisaf MS. Evacetrapib And Cardiovascular Outcomes: Reasons For Lack Of Efficacy. *J Thorac Dis.* 2017;9(8):2308-2310. Doi:10.21037/Jtd.2017.07.75.
10. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J; ASCOT Investigators. Prevention Of Coronary And Stroke Events With Atorvastatin In Hypertensive Patients Who Have Average Or Lower-Than-Average Cholesterol Concentrations, In The Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): A Multicentre Randomised Controlled Trial. *Lancet.* 2003 Apr 5; 361(9364):1149-58. Doi: 10.1016/S0140-6736(03)12948-0.
11. Kato ET, Cannon CP, Blazing MA, Bohula E, Guneri S, White JA, Murphy SA, Park JG, Braunwald E, Giugliano RP. Efficacy And Safety Of Adding Ezetimibe To Statin Therapy Among Women And Men: Insight From IMPROVE-IT (Improved Reduction Of Outcomes: Vytorin Efficacy International Trial). *J Am Heart Assoc.* 2017 Nov 18;6(11):E006901. Doi: 10.1161/JAHA.117.006901.
12. HPS2-THRIVE Collaborative Group. HPS2-THRIVE Randomized Placebo-Controlled Trial In 25 673 High-Risk Patients Of ER Niacin/Laropiprant: Trial Design, Pre-Specified Muscle And Liver Outcomes, And Reasons For Stopping Study Treatment. *Eur Heart J.* 2013 May;34(17):1279-91. Doi: 10.1093/Eurheartj/Eht055. Epub 2013 Feb 26.
13. Dubroff R. Cholesterol Paradox: A Correlate Does Not A Surrogate Make. *Evid Based Med.* 2017 Mar;22(1):15-19. Doi: 10.1136/Ebmed-2016-110602. Epub 2016 Dec 20. PMID: 27998881.
14. Mach F, Ray KK, Wiklund O, Et Al. Adverse Effects Of Statin Therapy: Perception Vs. The Evidence - Focus On Glucose Homeostasis, Cognitive, Renal And Hepatic Function, Haemorrhagic Stroke And Cataract. *Eur Heart J.* 2018;39(27):2526-2539. Doi:10.1093/Eurheartj/Ehy182.
15. Tamanna N, Mahmood N. Food Processing And Maillard Reaction Products: Effect On Human Health And Nutrition. *Int J Food Sci.* 2015;2015:526762. Doi:10.1155/2015/526762.
16. Srour B, Fezeu LK, Kesse-Guyot E, Et Al. Ultra-Processed Food Intake And Risk Of Cardiovascular Disease: Prospective Cohort Study (Nutrinet-Santé). *BMJ.* 2019;365:L1451. Published 2019 May 29. Doi:10.1136/Bmj.L1451.
17. Yu E, Malik VS, Hu FB. Cardiovascular Disease Prevention By Diet Modification: JACC Health Promotion Series. *J Am Coll Cardiol.* 2018;72(8):914-926. Doi:10.1016/J.Jacc.2018.02.085.
18. Cawthorn WP, Sethi JK. TNF-Alpha And Adipocyte Biology. *FEBS Lett.* 2008;582(1):117-131. Doi:10.1016/J.Febslet.2007.11.051.
19. Smith CS, Cannon CP, McCabe CH, Murphy SA, Bentley J, Braunwald E. Early Initiation Of Lipid-Lowering Therapy For Acute Coronary Syndromes Improves Compliance With Guideline Recommendations: Observations From The Orbofiban In Patients With Unstable Coronary Syndromes (OPUS-TIMI 16) Trial. *Am Heart J.* 2005 Mar;149(3):444-50. Doi: 10.1016/J.Ahj.2004.06.033.
20. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Shay CM, Spartano NL, Stokes A, Tirschwell DL, Vanwagner LB, Tsao CW; American Heart Association Council On Epidemiology And Prevention Statistics Committee And Stroke Statistics Subcommittee. Heart Disease And Stroke Statistics-2020 Update: A Report From The American Heart Association. *Circulation.* 2020 Mar 3;141(9):E139-E596. Doi: 10.1161/CIR.0000000000000757. Epub 2020 Jan 29. PMID: 31992061.
21. Budzyński J, Tojek K, Wustrau B, Et Al. The "Cholesterol Paradox" Among Inpatients - Retrospective Analysis Of Medical Documentation. *Arch Med Sci Atheroscler Dis.* 2018;3:E46-E57. Published 2018 Mar 27. Doi:10.5114/Amsad.2018.74736.
22. Rafieian-Kopaei M, Setorki M, Doudi M, Baradaran A, Nasri H. Atherosclerosis: Process, Indicators, Risk Factors And New Hopes. *Int J Prev Med.* 2014;5(8):927-946.
23. Saeed A, Kampangkaew J, Nambi V. Prevention Of Cardiovascular Disease In Women. *Methodist Debakey Cardiovasc J.* 2017;13(4):185-192. Doi:10.14797/Mdcj-13-4-185.
24. Iorga A, Cunningham CM, Moazeni S, Ruffenach G, Umar S, Eghbali M. The Protective Role Of Estrogen And Estrogen Receptors In Cardiovascular Disease And The Controversial Use Of Estrogen Therapy. *Biol Sex Differ.* 2017;8(1):33. Published 2017 Oct 24. Doi:10.1186/S13293-017-0152-8.
25. Jabri A, Kumar A, Verghese E, Alameh A, Kumar A, Khan MS, Khan SU, Michos ED, Kapadia SR, Reed GW, Kalra A. Meta-Analysis Of Effect Of Vegetarian Diet On Ischemic Heart Disease And All-Cause Mortality. *Am J Prev Cardiol.* 2021 Apr 9;7:100182. Doi: 10.1016/J.Ajpc.2021.100182.

26. Poursafa P, Moosazadeh M, Abedini E, Et Al. A Systematic Review On The Effects Of Polycyclic Aromatic Hydrocarbons On Cardiometabolic Impairment. *Int J Prev Med.* 2017;8:19. Published 2017 Apr 6. Doi:10.4103/Ijpvvm.IJPVM_144_17.
27. Manchanda SC, Passi SJ. Selecting Healthy Edible Oil In The Indian Context. *Indian Heart J.* 2016;68(4):447-449. Doi:10.1016/J.Ihj.2016.05.004.
28. Srour B, Fezeu LK, Kesse-Guyot E, Allès B, Méjean C, Andrianasolo RM, Chazelas E, Deschasaux M, Hercberg S, Galan P, Monteiro CA, Julia C, Touvier M. Ultra-Processed Food Intake And Risk Of Cardiovascular Disease: Prospective Cohort Study (Nutrinet-Santé). *BMJ.* 2019 May 29;365:L1451. Doi: 10.1136/Bmj.L1451.
29. Pacheco LS, Lacey JV Jr, Martinez ME, Lemus H, Araneta MRG, Sears DD, Talavera GA, Anderson CAM. Sugar-Sweetened Beverage Intake And Cardiovascular Disease Risk In The California Teachers Study. *J Am Heart Assoc.* 2020 May 18;9(10):E014883. Doi: 10.1161/JAHA.119.014883. Epub 2020 May 13. PMID: 32397792; PMCID: PMC7660873.
30. Al-Shaar L, Satija A, Wang DD, Rimm EB, Smith-Warner SA, Stampfer MJ, Hu FB, Willett WC. Red Meat Intake And Risk Of Coronary Heart Disease Among US Men: Prospective Cohort Study. *BMJ.* 2020 Dec 2;371:M4141. Doi: 10.1136/Bmj.M4141. PMID: 33268459; PMCID: PMC8030119.
31. Zhang B, Xiong K, Cai J, Ma A. Fish Consumption And Coronary Heart Disease: A Meta-Analysis. *Nutrients.* 2020 Jul 29;12(8):2278. Doi: 10.3390/Nu12082278. PMID: 32751304; PMCID: PMC7468748.
32. London B., Albert C., Anderson M.E., Giles W.R., Van Wagoner D.R., Balk E., Billman G.E., Chung M., Lands W., Leaf A., Et Al. Omega-3 Fatty Acids And Cardiac Arrhythmias: Prior Studies And Recommendations For Future Research: A Report From The National Heart, Lung, And Blood Institute And Office Of Dietary Supplements Omega-3 Fatty Acids And Their Role In Cardiac Arrhythmogenesis Workshop. *Circulation.* 2007;116:E320–E335.
33. Aune D, Giovannucci E, Boffetta P, Fadnes LT, Keum N, Norat T, Greenwood DC, Riboli E, Vatten LJ, Tonstad S. Fruit And Vegetable Intake And The Risk Of Cardiovascular Disease, Total Cancer And All-Cause Mortality-A Systematic Review And Dose-Response Meta-Analysis Of Prospective Studies. *Int J Epidemiol.* 2017 Jun 1;46(3):1029-1056. Doi: 10.1093/Ije/Dyw319. PMID: 28338764; PMCID: PMC5837313.
34. Kopčėková, J., Holovičová, M., Gažarová, M., Mrázová, J., Habánová, M., Mečiarová, L., & Bronkowska, M. (2020). Association Between Selected Dietary Habits And Lipid Profiles Of Patients With Cardiovascular Disease. *International Journal Of Environmental Research And Public Health*, 17(20), 7605. <https://doi.org/10.3390/Ijerph17207605>.
35. Popkin BM, Adair LS, Ng SW. Global Nutrition Transition And The Pandemic Of Obesity In Developing Countries. *Nutr Rev.* 2012;70:3–21.
36. Bhupathiraju SN, Tobias DK, Malik VS, Et Al. Glycemic Index, Glycemic Load, And Risk Of Type 2 Diabetes: Results From 3 Large US Cohorts And An Updated Meta-Analysis. *Am J Clin Nutr.* 2014;100:218–232.
37. R. S. Venkatesh And Zaheda Bano. A Survey On Risk Assessment Among Populations After Following Keto Diet. *Int J Pharm Bio Sci.* 2019; 9(4): 41-43.
38. Mirrahimi A, De Souza RJ, Chiavaroli L, Et Al. Associations Of Glycemic Index And Load With Coronary Heart Disease Events: A Systematic Review And Meta-Analysis Of Prospective Cohorts. *J Am Heart Assoc.* 2012;1:E000752.
39. Mensink RP, Zock PL, Kester AD, Katan MB. Effects Of Dietary Fatty Acids And Carbohydrates On The Ratio Of Serum Total To HDL Cholesterol And On Serum Lipids And Apolipoproteins: A Meta-Analysis Of 60 Controlled Trials. *Am J Clin Nutr.* 2003;77:1146–55.