Original Study

IS A REFINED VEGETABLE OILS A RISK FACTOR FOR RECURRENCE OF CORONARY ARTERY DISEASES AND HYPERCHOLESTEROLEMIA? A RETROSPECTIVE COHORT STUDY ON 107 PATIENTS

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ABSTRACT

Aim: The primary purpose of this study was to verify the effect of the refined vegetable oils on recurrence of coronary artery disease (CAD) and hypercholesterolemia (HC).

Materials and methods: The retrospective cohort study was conducted on 140 sequential patients admitted and diagnosed with CAD and HC in a rural medical institute in Udaipur, Rajasthan, India. The complete medical case files were examined through the study investigators and relative findings were noted. The patient's exposure to the refined vegetable oils were assessed via questioning; which was mainly divided into two groups as 'exposed group', those who were continued on the refined vegetable oils consumption and 'non-exposed group' , those who were stopped along with 6 month follow up for evaluation of recurrence of CAD and HC scheduled. CAD recurrence and HC recurrence were considered as the outcomes. The effect of the refined vegetable oils on recurrence of CAD and HC were investigated according to a logistic regression model.

Results: Total 107 patients fulfilled the inclusion criteria; 63 patients were in the 'exposed group'. The 6-month follow up results were the refined vegetable oils consumption a 34.93 times the odds of hypercholesterolemia recurrence (P = 0.017; 95% CI for OR ranged from 1.90 to 643.46), while 26.60 times the odds of coronary artery diseases recurrence (P = 0.003; 95% CI for OR ranged from 3.04 to 232.62) in exposed and non-exposed group which were statistically significance difference found.

Conclusion: Refined vegetable oils tends to increase the risk of recurrence of coronary artery disease and hypercholesterolemia.

KEYWORDS Cohort study, Coronary artery diseases, Hypercholesterolemia, Refined vegetable oil, Trans fat.

INTRODUCTION

Coronary artery disease (CAD) is also known as the ischemic heart disease (IHD)[1], CADs are a group of diseases that include stable angina, unstable angina, myocardial infarction and sudden cardiac death[2]. CAD is the most common type within the group of cardiovascular diseases (CVDs) [3]. Hypercholesterolemia (HC) is also known as dyslipidemia, which refers to presence of high levels of cholesterol in the blood. And it's the form of high blood lipids and hyperlipoproteinemia, means of elevated levels of lipoproteins in the blood[6]. Vegetable oil is nothing but the triglyceride that is extracted from

the plant[4]. The refined vegetable oil is obtained from the seeds of various plant sources and fats from plant seeds, which are mainly polyunsaturated. Commercially, the different kinds of refined vegetable oils are soybean oil, canola oil, corn oil, sunflower oil, safflower oil, peanut oil, etc.[5] World-widely, CAD is one of the main cause of death not only in the developed countries but also increasingly in developing countries like India[7]. The risk factors for CAD were not formally established until the findings of the Framingham Heart Study (early 1960s) were released[5]. Commonly, the important systemic risk factors for CAD and HC is considered as the worst prognosis are diabetes[8], obesity[9], metabolic syndrome[10] and cigarette smoking[11]. The cessation of cigarette smoking is a single most important preventive measure for CAD and HC[5]. Some of the systemic conditions are as end stage renal disease (ESRD)[5], chronic inflammatory diseases affecting connective tissues for examples of lupus, rheumatoid arthritis,etc[12,13], HIV infection[(AIDS) and highly active antiretroviral therapy(HAART)][14], Xanthelasmata[11] as observed in CAD and HC. Thus, the understanding of risk factors and its stratification is important for any clinician to prevent the cardiovascular morbidities and mortality[11]. The search on PubMed or Medline or Google Scholar was performed along with matching random combinations of the terms 'refined vegetable oils' or 'vegetable oils' or 'Trans Fat' or 'high Cholesterol' with the terms 'Coronary artery disease' or 'hypercholesterolemia' or 'cholesterolaemia' or 'dyslipidaemia' or 'hyperlipidaemia'. In one of the recent review[9], based on the studies on food consumption and its effects on CAD and HC recommended the preventive approach of a traditional Mediterranean-type diet which includes plant foods or emphasizes plant protein sources, which ultimately provides a tested healthy dietary pattern to reduce the CAD and HC. The references of this paper were screened and no clinical studies were found. Research regarding the vegetable oil highlights the influence of total serum cholesterol level on CAD and HC. A risk factor research is usually based on the observational studies like as case series or cross-sectional studies are the first step for generating any hypothesis, with case-control or cohort studies which used to evaluate cause and effect relationships. Commonly, the cohort studies are prospective in direction but a retrospective study can be conducted if the measurement of exposure is taken before onset of the disease[16]. The purpose of this study was to test the hypothesis that the refined vegetable oils which were considered in the study as the after its consumption, total cholesterol (TC) level increases among CAD and HC patients, plays a role in recurrence of signs and symptoms of CAD and HC, via a retrospective cohort study.

MATERIALS AND METHODS

Study Design

This study was designed as a retrospective cohort study, mainly focusing on the effect of the refined vegetable oils on the recurrence of CAD and HC. This report was drawn up according to the STROBE checklist (STrengthening the Reporting of Observational Studies in Epidemiology) statement[17] which was recommended for the observational studies.

Official permission, Ethical clearance and Informed consent

An official permission was obtained from Pacific institute of medical science, Umarda, Udaipur, Rajasthan, India. The study protocol was reviewed by Ethical Committee of Pacific Dental College and Hospital, Udaipur, Rajasthan, India and the ethical clearance was granted for the study. After explaining the purpose and details of the study, the informed consent was obtained from the included patients of the study, who were willing to participate.

Setting and Participants

The study was carried out by sorting of data from the patients undergoing treatment in our rural medical institute in Udaipur city, Rajasthan, India. All patients suffering from CAD and HC, who were admitted and undergoing the treatment between December 2014 and December 2015 were considered eligible. After the treatment, readmitted patients with CAD and HC, a six month follow up period was considered for all patient and this follow up visits were scheduled between December 2014 and December 2016. The data were collected and analysed between January and February 2017 in different visits. In the practice, every patients who underwent the CAD and HC treatment were evaluated for different findings and no treatment or any surgery was performed, if the systemic findings were not under control. The patients who were stabilised with most common systemic risk factors like diabetes, hypertension and smoking were included in our study. So as the refined vegetable oil was the only hypothetic risk factor exposed during the follow up and then results were awaited. Furthermore, all patients must had a medical and diet history, in which they were asked to specify details concerning diet consumption specially refined vegetable oils, along with other relevant information. Subsequently, the general status of all patients

were conducted before treatment by means of blood tests including TC levels and glucose levels and also an electrocardiogram (ECG) were seen. After that; medical and diet history, blood tests, ECG reports and other available reports were scanned and noted. Within the group of eligible patients, only the ones whose scanned files included with medical and diet history, blood tests and ECG reports were selected. Furthermore, patients not undergoing treatment or who were non-compliant with follow up program of institution were excluded from the study.

Variables and data sources

The Data about dietary habits especially refined vegetable oils consumption, diabetes, hypertension, smoke habits were collected from patient files. The first factor was considered as the exposure and the last three factors were considered as the effect analysers, as they are the only systemic factors for which, so far, an evident association with refined vegetable oil consumption and recurrence of CAD and HC has been demonstrated. TC level < 200 mg/dl were considered to be normal, with patients who showed higher values be considered Hypercholesterlaemic[24, 25] and subsequent CAD. Patients suffering from uncontrolled diabetics were excluded from the study, no patients showed glucose levels higher than 130 mg/dl. Patients were then divided into patients with normal glucose levels considered as less than 100 mg/dl fasting glucose and patients with impaired fasting glucose as from 100 mg/dl to 125 mg/dl fasting glucose. A six month follow up was considered all patients. Finally, the outcomes taken into consideration was the recurrence of CAD and HC. All findings were registered in both patient's file and in a special register. Patient's final collected data in the file and special register were then matched in order to cross-check recurrence events.

Statistical Methods

The univitiate effect of refined vegetable oils consumption on recurrence of CAD and HC was investigated via a logistic regression model. The odds ratio (OR) and related 95% CI based on robust standard error were computed and Wald chi square test was applied to evaluate factor significance. Furthermore, the analysis was performed at patient level. The data were considered statistically significant for $P < 0.05$. The independent variable refined vegetable oils consumption as exposure was categorised either '0' exposed group or '1' non-exposed group in both analyses. Diabetes, Hypertension, Smoke habit were initially analysed and were found that they do not significantly modify the exposed and non-exposed group. For the complete analysis, every model was repeated with and without these systemic factors. The logistic regression model was performed with SPSS, version 20.0[SPSS Inc. Chicago, ILLNOIS, USA].

Table 1: Comparing demographic and clinical features of the two cohorts:

Refined vegetable oils consumption	Exposed group	Non-Exposed group	Total
Number of Patients	63	44	107
Age (standard deviation)	53.6 (12.9)	59.1 (10.1)	56.9 (11.6)
Male : Female ratio	33 : 32	24 : 20	57 : 52
Smokers	17	10	27
Impaired fasting glucose	9	5	14
Hypertensive	13	9	22
Total effect modifiers	39	24	63
Total without effect modifiers	24	20	44

Note: effect modifiers – smokers, impaired fasting glucose, hypertensive.

RESULT

Of the 140, 109 patients which were eligible for the study, 31 were excluded, because exhaustive original scanned files and reports were not available and 2 patients who died during the further treatment due to severity of disease. Thus, the total 107 patients were included in the study. All patients were observed in the institute for six months follow up and all 107 patient's data were analysed, out of them 53.27% were men and 48.60% were women. Out of 107 patients, 63(58.88%) were exposed to refined vegetable oil, 14(13.08 %) suffered from impaired fasting glucose, 22(20.56%) were hypertensive, 27(25.23%) were smokers. Table 1 compares demographic and clinical features of the two

cohorts. Within the population of exposed group, HC recurrence occurred in 9 of 39 patients, which meant a cumulative six month follow up recurrence rate of 23.08% at patient level and CAD recurrence occurred in 3 out of 39 patients with six month follow up recurrence rate 7.69% at patient level (Table 2). While no patient seen with recurrence of CAD and HC in exposed or non-exposed group along with effect modifiers. The logistic regression model with systemic factors that are impaired glycaemia, hypertension and smoke habits did not highlight any statistical significance on CAD recurrence (P = 0.065, Table 2) and HC recurrence (P = 0.313, Table 2). The refined vegetable oils consumption effect rate was close to statistically significant in exposed and non-exposed group a 15.26 greater odds of HC recurrence (P = 0.065; 95% CI for OR ranged from 0.85 to 275.49, Table 2); and was not statistically significant in exposed and non-exposed group a 4.7 greater odds of CAD recurrence (P = 0.0313; 95% CI for OR ranged from 0.23 to 95.05, Table 2). In smokers, hyperglycaemic and hypertensive, no statistical significance was reported so as it did not alter the risk of recurrence of HC (OR = 5.07, P = 0.300; OR =3.67, P = 0.430; and OR = 9.00, P = 0.159 respectively; Table 2a) or recurrence of CAD (OR = 1.91, P = 0.700; OR = 0.58, P = 0.792; and OR = 4.13, P = 0.375 respectively Table 2b). Repeating the analysis without the systemic factor, the recurrence effect was similar, in fact, the relationship between refined vegetable oils consumption in exposed and non-exposed group on recurrence of CAD and HC was statistically significant (P = 0.017 and P = 0.003 respectively; Table 3). The refined vegetable oils consumption effect rate was seen in exposed and non-exposed group a 34.93 greater odds of HC recurrence (P = 0.017; 95% CI for OR ranged from 1.90 to 643.46) and was not statistically significant in exposed and non-exposed group a 26.60 greater odds of CAD recurrence (P = 0.003; 95% CI for OR ranged from 3.04 to 232.62). Thus, even without the modifiers, the effect of the refined

Table 2: Effect of refined vegetable oils consumption on recurrence of hypercholesterolemia and coronary artery diseases (Logistic regression model with effect modifiers):

	Seen/Absent in Exposed group	Seen/Absent in Non-Exposed group	Odd Ratio (OR)	95% CI	P-value
Hypercholesterolemia recurrence	9/30	0/24	15.26	0.85 to 275.49	P = 0.065
Coronary artery diseases recurrence	3/36	0/24	4.70	0.23 to 95.05	P = 0.313

Note: OD - odd ratio, CI - confidence level, P-value - level of significance.

Table 2a: Effect of systemic factors on hypercholesterolemia recurrence (Logistic regression model with effect modifiers):

	Odd Ratio (OR)	95% CI	P-value
Refined vegetable oils consumption	15.26	0.85 to 275.49	P = 0.065
Smokers	5.07	0.24 to 108.96	P = 0.300
Hyperglycaemic	3.67	0.15 to 92.66	P = 0.430
Hypertensive	9.00	0.42 to 191.39	P = 0.159

Note: OD - odd ratio, CI - confidence level, P-value - level of significance.

Table 2b: Effect of systemic factors on coronary artery diseases recurrence (Logistic regression model with effect modifiers):

	Odd Ratio (OR)	95% CI	P-value
Refined vegetable oils consumption	4.70	0.23 to 95.05	P = 0.313
Smokers	1.91	0.07 to 51.39	P = 0.700
Hyperglycaemic	0.58	0.01 to 33.51	P = 0.792
Hypertensive	4.13	0.18 to 96.94	P = 0.378

Note: OD - odd ratio, CI - confidence level, P-value - level of significance.

Table 3: Effect of refined vegetable oil consumption on recurrence of hypercholesterolemia and coronary artery disease (Logistic regression model without effect modifiers):

	Seen/Absent in Exposed group	Seen/Absent in Non-Exposed group	Odd Ratio (OR)	95% CI	P-value
Hypercholesterolemia recurrence	11/13	0/20	34.93	1.90 to 643.46	P = 0.017*
Coronary artery diseases recurrence	14/10	1/19	26.60	3.04 to 232.62	P = 0.003*

vegetable oils consumption remained the same in both on recurrence of CAD and HC.

DISCUSSION

The aim of the study was to evaluate the effect of refined vegetable oil on recurrence of coronary artery disease and hypercholesterolemia. The analysis highlighted a significance tendency for patients with refined vegetable oil consumption to have recurrence of coronary artery disease and hypercholesterolemia (Table 2; a model with effect modifiers and Table 3; a model without effect modifiers). Cohort study approach chosen for this work might be questioned because of retrospective design. In the context of observational studies, cohort and case-control studies are used to verify hypotheses and to assess the causality. The cohort studies select individuals on the basis of exposure conditions and, in most of the cases, they are prospective. Nevertheless, cohort studies can also be retrospective, when the exposure measurements are taken before the onset of a disease[26]. As, in the present study, all data relating to the exposure to systemic risk factors, whether it is refined vegetable oils consumption or effect modifiers, were acquired and filed before the further treatment or surgery. In our analysis, all systemic factors that have been demonstrated to be related to recurrence of CAD and HC were considered as effect modifiers. No patients with uncontrolled diabetes were included, because in our practice such patients are not eligible for further treatment or surgery before appropriate glycaemic control has been obtained. Patients were then divided into 2 groups as patients with normal glucose and patients with impaired fasting glucose. Some other uncommon factors, which have been previously described, such as end stage renal disease (ESRD), chronic inflammatory diseases affecting connective tissues for examples of lupus, rheumatoid arthritis, etc. , HIV infection[(AIDS) and highly active antiretroviral therapy(HAART)], and Xanthelasmata were not considered, and no patients in both cohorts were affected by them[11 to 14] In metabolic studies shown that trans-fat have adverse effect on blood TC level as increasing LDL ("bad") cholesterol while decreasing HDL("good") cholesterol[12]. The relation between trans-fat and risk of coronary heart disease had been reported from three large cohort studies, HPFS study, ATBC study ,NHS study[19, 20, and 21]. In these studies, trans fat consumption was assessed using detailed food frequency questionnaire (FFQ) that were finally validated by comparing adipose composition or several days of diet records[22]. Trans-fat mainly can be found in the vegetable oils, partially hydrogenated during refining[23]. Therefore, the refined vegetable oils consumption can be directly or indirectly related to increasing trans-fat which ultimately increases LDL cholesterol. A further limitation of this study is the fact that evaluation of cholesterol levels only considers TC levels. LDL cholesterol levels, which are the actual factor associated with refine vegetable oil consumption, were not considered, due to the lack of data on it. It is important to underline that, in fasting blood tests[23], TC levels are good indicators of LDL levels. In fact, this study showing a direct association between increase cholesterol level (due to consumption of refined vegetable oil) and recurrence of coronary artery disease and hypercholesterolemia, such an association is the same for both TC and LDL-C levels.

CONCLUSION

In final conclusion, in this retrospective cohort study we found a significant association between refined vegetable oil consumption and recurrence of coronary artery diseases and hypercholesterolemia. Despite the limitations of this study, it can be suggested that evaluation of refined vegetable oil consumption could be advisable before relevant coronary artery diseases or hypercholesterolemia treatment procedures are performed. The prospective studies with larger sample sizes will be useful in confirming the findings.

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