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COMPARATIVE STUDY OF LIPID PROFILE OF SMOKERS AND NON-SMOKERS PRESENTING WITH ACUTE CORONARY SYNDROME

Cardiology

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ABSTRACT

Introduction- Objectives of the study are to study the lipid profiles in young smokers and non-smokers presenting with first onset of acute coronary syndrome and their comparison and study the effect of smoking on the presentation and outcome of acute coronary syndrome and, to study the effect of lipid profile on the presentation and outcome of acute coronary syndrome.

Methodology- This is prospective case-control study. All data collected was compared between three groups- non-smokers, ex-smoker, current-smokers. studied these young men with no previous history of heart disease or co-morbid condition between age 20-40 years and were screened. Their physical activity, smoking habits, presenting symptoms, vitals, history of microalbuminuria, changes in the electrocardiogram (ECG), ST segment deviation, serum lipids, troponin I values, fasting lipid profile, total blood count, serum electrolytes, Echocardiographic and angiographic evaluation and clinical outcome was recorded and analysed. Various statistical tests such as chi square test, p values, ANNOVA test, t-test were performed using SPSS software.

Result- Incidence of dyslipidaemia was found to be more in patients with sedentary physical activity and was lowest in those with heavy physical activity. 50% of patients with NSTEMI were non-smokers and almost all patients with STEMI were either ex-smokers or current smokers, though >3/4th patients were current smokers. In ex-smokers and current smokers, presence of occlusive disease was more common with angiogram showing SVD / DVD / TVD in majority of patients, indicating more severe disease. Almost all deaths occurred in patients with TVD. Dyslipidaemia (elevated TC, TG & LDL and reduced HDL) was seen more in current smokers compared to ex-smokers and non-smokers. Current smoker group had a greater number of patients with low ejection fraction as compared to non-smoker group. Highest mortality was seen in current smokers.

Conclusion- Incidence of incidence of ACS increases with age and is more in current-smokers than in non-smokers. Morbidity and mortality were seen to be directly related to age, years of smoking, total cholesterol, LDL- cholesterol, total cholesterol / HDL ratio, troponin I elevation, STEMI, conduction defect, amount of ST segment deviation, and extent of CAD. Employment of organized programs and aggressive steps are needed for mass education and awareness regarding smoking and smoking related risk to health. Smoking cessation activities should be encouraged.

KEYWORDS

Smoking status, lipids, NSTEMI, LDL, HDL

INTRODUCTION

Coronary artery disease (CAD) is one of the major health problems associated with increasing mortality and morbidity in the Indian subcontinent as well as in ethnic Indian communities all over the world.[1] It continues to be one of the major causes of death in industrialized countries, atherosclerosis being its etiopathogenic substrate.[2] Acute myocardial infarction with no previous angina has been suggested to be more prevalent in young males.[3, 4, 5] According to the literature; acute myocardial infarction is the first manifestation of ischemic heart disease in approximately 50% to 70% of patients.[6, 7] The etiopathogenesis of CAD is multifactorial. Several risk factors for the disease are as follows: age, sex, smoking, obesity, physical inactivity, emotional stress, systemic arterial hypertension, diabetes mellitus, and dyslipidemia.[8] It has not yet been established whether any of the risk factors have an independent participation in the instability of the plaque for triggering myocardial infarction as the first manifestation of ischemic heart disease.[9]

Smoking is the most important risk factor for CAD in young subjects.[10, 11] Most of epidemiological data in single and cross-cultural populations, have strongly linked tobacco smoking, hypertension, elevated total and low-density lipoprotein (LDL) cholesterol to the subsequent development of CAD.[12, 13] There is a dose response relationship between the number of cigarettes/ bidis smoked and cardiovascular morbidity and mortality.[14,15] Smoking increases total cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol and causes fall in the levels of antiatherogenic HDL-cholesterol, as reported by various workers[16,17,18,19]. It is also believed that modification of LDL increases its atherogenicity[20]. The free radicals alter the lipid metabolism and form oxidized and cytotoxic LDL, which is considerably more atherogenic than native LDL. Mechanisms proposed in lipid alteration by smoking are: 1) Nicotine stimulates adrenal sympathetic system leading to increased secretion of catecholamines resulting in increased lipolysis and increased concentration of plasma free fatty acids (FFA) which further result in increased secretion of hepatic FFAs and hepatic triglycerides along with VLDL-Cholesterol in the blood stream.[21,22] 2) Fall in estrogen levels which leads to decreased HDL-Cholesterol.[23] 3) Presence of hyperinsulinemia in smokers leads to increased total cholesterol, LDL-Cholesterol, VLDL-Cholesterol, and TG due to decreased activity of lipoprotein lipase.3) Consumption of a diet rich in fat and cholesterol as well as a diet low in fibre and cereal content by smokers as compared to non-smoker.[24]

Aim of this research was to study and compare the lipid profiles in young smokers and non-smokers presenting with first onset of acute coronary syndrome.

MATERIALS AND METHODS-

The prospective case-control study was carried out in Malabar Institute of Medical Sciences, Calicut, Kerala. Males (non-smokers & smokers) in the age group 21-40 years presenting with first episode of acute coronary syndrome admitted during last 16 months in the hospital. Institutional ethical committee approval was taken.

Female patients, patients with ethanol use, history of diabetes mellitus, obesity, history of systemic hypertension and any previous heart disease were excluded. History of smoking, duration and number of cigarettes/ bidis smoked/day, height and weight was evaluated in each subject. They were examined clinically as well as through a battery of investigation and data were collected in a data sheet. Criteria for defining cases were- current smoker are more than 5 cigarettes / bidis per day currently for more than 6 months. Non-smokers are those who never smoked. Ex-smokers who have left smoking 2 years back.[25] All data collected was compared between three groups- non-smokers, ex-smoker, current-smokers. Dyslipidemia was defined according to

WHO criteria[26]- Triglycerides >150 mg/dl, HDL-cholesterol <40 mg/dl. We therefore studied these young men with no previous history of heart disease or co-morbid condition between age 20-40 years and were screened. Their physical activity, smoking habits, presenting symptoms, vitals, history of microalbuminuria, changes in the electrocardiogram (ECG), ST segment deviation, serum lipids, troponin I values, fasting lipid profile, total blood count, serum electrolytes, Echocardiographic and angiographic evaluation and clinical outcome was recorded and analyzed. Various statistical tests such as chi square test, p values, ANNOVA test, t-test were performed using SPSS software.

RESULTS

1532 patients were admitted with acute coronary syndrome during the study period around of which 101 patients were eligible for our study. In the study, out of 101 patients, 5.9 % were from age group <=25 years, 4% from 26-30 years of age, 19.80 % were from 31-35 years of age and 70.3% were from 36-40years. Out of total 101 patients, 74.3% were smokers (ex-smokers and current-smokers) and 25.7% were non-smokers. Majority of smokers belonged to 31-40 years age group.

In the study maximum number of patients were found to have sedentary physical activity (47.5%). 27.70 % and 24.80% were from moderate physical activity and heavy physical activity respectively. And patients with sedentary physical activity were in large number (31.7%) in age group of 36-40 years. It was found that the incidence of ACS was highest in patients with sedentary physical activity (47.50%) and lowest in those with heavy physical activity (24.85%) Below the age of 30 years, only 9 % of patients had dyslipidemia. 66.3% of patients from age group 36-40 years had dyslipidaemia. Incidence of dyslipidemia in these patients with acute coronary syndrome was 92.1% and 7.9% were found to have normal lipids. Out of 48 patients with sedentary physical activity, 45 patients had dyslipidemia. Out of 25 patients with ACS and heavy physical activity, 23 had dyslipidemia. Out of 93 patients with dyslipidemia, 45 had sedentary physical activity, 23 had heavy physical activity. Incidence of dyslipidemia was found to be more in patients with sedentary physical activity and was lowest in those with heavy physical activity.

Out of 101 patients, majority of patients 62(61.4%) were current smokers. 13(12.9%) and 26(25.7%) of patients were ex-smokers and non-smokers respectively. Most of the patients presented with typical chest pain [92 (91.1%)]. Some [9(8.9%)] had atypical chest pain at presentation. Incidence of Non-ST Elevation Myocardial Infarction-(NSTEMI) was 51.5% and that of ST Elevation Myocardial Infarction (STEMI) was 48.5% in our study. 50 % of NSTEMI were found in non-smokers and 78 % of STEMI were found in current smokers. Anterior wall hypokinesia was seen in 37.6 % of patients followed by lateral and inferior wall in 15.8 % and 35.6 % of patients respectively.

Among 26 non-smokers, 13 (50%) had elevated total cholesterol, 12(46.1%) had elevated triglycerides and 12 (46.1%) had elevated LDL levels and 17 (65.3%) were found to have low HDL levels. Among 13 ex-smokers 11 (84.6%) had elevated total cholesterol, 10 (76.9%) had elevated triglycerides and 8 (61.5%) had elevated LDL levels and only 5 (38.4%) were found to have low HDL levels. While Among 62 current-smokers, 44 (70.9%) had elevated total cholesterol and elevated LDL levels and only 49 (79%) were found to have low HDL (High density level) levels but 34 (54.8%) patients were found to have hypertriglyceridemia. Total cholesterol was elevated (i.e.> 200mg/dl) in 71% of current smokers, 84.60% of exsmokers and 50% of nonsmokers. 71% of current smokers and 62.5% of ex-smokers were found to have very high LDL, while only 42.3 % of nonsmokers had high LDL.

Dyslipidemia (total cholesterol >=200mg/dl, TG>=150mg/dl, LDL>=130, and/or HDL< 40mg/dl) was significantly seen in 80% of non-smokers, all ex-smokers and 95.20 % of current smokers, p value <0.05. Among patients with elevated cholesterol, 64 % were current smokers and 20 % were non-smokers. In patient having hypertriglyceridemia, 60 % were found to be current smokers 22% were non-smokers. In patients found to have low HDL, 64 % were current smokers and 21 % were non-smokers. In 64 patients with high LDL levels, 68 % were smokers and only 19 % were non-smokers. 50 % of non-smokers, 84.6 % of ex-smokers, and 74.2% of current-smokers were found to have elevated total cholesterol and HDL ratio.

Table 1 shows that current smoker patients had significant increase in ST segment deviation than non-smoker and ex-smoker, p <0.05. Troponin I values were significantly elevated in most of current smokers while in nonsmokers, most had minimal Troponin I elevation, p value<0.05.

Table 1. Comparison of smoking status and ST segment deviation

ST segment deviation	0.4 – 2mm	2.0 - 4.0mm	> 10mm	P value
Non-smoker	17(16.80%)	4(4%)	5(5%)	<0.05
Ex smoker	7(6.90%)	6(5.90%)	0(0%)	
Current smoker	10(9.90%)	28(27.70%)	24(23.80%)	

As seen in table 2, non-smokers, 1% had low ejection fraction (EF<=40%). In ex-smokers and current smokers, 1% and 20.8% of patients were found to have low ejection fraction (EF<=40%), p value <0.05.

Table 2. Comparison of Ejection fraction and smoking status

Smoking status	EF>=40	EF<40	P value
Non-smoker	25(24.80%)	1(1%)	<0.05
Current-smoker	41(40.60%)	21(20.80%)	
Ex-smoker	12(11.90%)	1(1%)	

On angiographic evaluation, 38.5% of non-smokers were found to have normal angiogram while 46% had single vessel disease. Among ex-smokers, 30.8% and 46.2% of patients were found to have single and double vessel disease respectively. Among current smokers 43.5% had single vessel disease and 30.6 % had double vessel disease. 14.5% current smokers had triple vessel disease, p value <0.05. Among current smokers, 52 out of 62 had maximum ST deviation more than 4mm. Among nonsmokers, 13 of 26 patient had maximum ST deviation between 4-8mm and no one had more than 8mm ST deviation. It was found that current smoker group had more patients with maximum ST segment deviation greater than 4 mm than non-smokers and ex-smokers. The difference was found to be statistically significant (P value <0.05) An angiography study, 20 patients had normal angiogram, 43 had SVD, 27 had DVD and 12 had TVD. In patients with normal angiogram, 11(57.90%) had maximum ST deviation <4mm and 8(42%) had ST deviation between 4-8mm. In patients with single vessels disease 32 out of 43 (74.40%) patients had maximum ST deviation > 4mm, and among patients having triple vessel disease out of 12, 11 (91.70%) patients had ST deviation more than 4mm (P value <0.05).

In the study group, comprising of 101 patients with Acute coronary syndrome(ACS), 5 patients died. 19% had normal Coronary angiography, 43 % had single vessel disease(SVD) and 27 % had double vessel disease(DVD). Triple vessel disease(TVD) was found in 12 % of patients. In patients with normal coronary angiogram, no mortality was found. In patients with single vessel disease and double vessel disease, 2% and 7% mortality were found. 17% of patients with triple vessel disease died during our study. In patients with <130 mg/dl, no mortality was found, but 8% mortality was found in patients with elevated LDL level. Out of 64 patients who had high LDL cholesterol, 5 patients died. In this study, 11 patients had documented conduction defects. In patients who had arrhythmias or conduction defects the mortality was comparatively higher especially in those with RBBB (28.6%) and LBBB (100.0%) . Patient with low EF (< 40%) had more number of patients with ST segment Deviation. Around 8% of patient had ST max deviation more than 8 mm in atleast 1 lead. Comparatively those who had good EF (> =40%), non one had ST deviation larger than 8 mm. It was found that, in patients who died of ACS, 40% of patients had maximum ST deviation more than 8 mm. Also those who died had more ST segment deviation. Among the survivors, only 6 % had maximum ST deviation of more than 8mm.

DISCUSSION

Incidence of ACS was highest in age group of 36-40 years than in any other age groups in our study, indicating that incidence of ACS increases as age increases. This is similar to the study conducted by CARDIA Coronary Artery disease in young adults,[27] Jalowiel DA and Hill JA et al [28] which showed less incidence in young patients, which progressively increases with age and a greater number of patients were seen in age > 35 years. It may be due to increase in the risk factors in later part of life, like increased stress, dyslipidemia, decreased physical activity, smoking habits. Incidence of ACS is more in current smokers than in ex-smokers & non-smokers. In our study, 3/4th of patients were either current smokers or ex-smokers. This is similar to the studies

conducted by Kannel W et al - Framingham heart study[29] which showed three times higher risk in smokers compared to non-smokers. Williams MJ et al[30] noted that 2 percent to 6 percent of MIs occur in young patients. Similar results are seen in studies done by Fournier JA et al.[31] Incidence is more in smokers due to predisposition for dyslipidemia, metabolic syndrome, atherosclerotic effects of nicotine and other smoking ingredients. In our study, incidence of STEMI and NSTEMI were almost similar. Most of the patients in the study presented with typical pain (91.10%). As age advances, the frequency of typical pain increases with atypical pain more common in younger age group. Dyslipidemia was found to be more in patients with age above 30 years with maximum prevalence between 36-40 years and least in age group < 30 years. It may be due to increased smoking activities, sedentary physical life, and newer risk factors in later life. The difference was found to be statistically significant. Incidence of dyslipidemia was found to be more in patients with sedentary physical activity and was lowest in those with heavy physical activity. This was found to be statistically significant. Sedentary physical activity was found to be more frequent in older patients with a peak prevalence in the age group 36-40 years of age. It increases with age. ACS is seen more commonly in patients with sedentary physical activity compared to patients with heavy physical activity. This data is comparable to the studies conducted by Witteman TC et[32], Williams MJ et al.[30] Sedentary physical activity predisposes to increased incidence of dyslipidemia and other metabolic syndromes with increased risk of thromboembolic phenomena. In our study the data analysis showed statistically significant difference between these two groups. Anterior wall MI is more commonly affected followed by inferior and lateral wall MI. It was comparable to study conducted by Fournier JA et al[31] who also found anterior inferior wall to be more affected in their case studies. On angiography, either no abnormality or SVD was found in majority of non-smokers, indicating milder disease. But in ex-smokers and current smokers, presence of occlusive disease was more common with angiogram showing SVD / DVD / TVD in majority of patients, indicating more severe disease. Almost all deaths occurred in patients with TVD. This is similar to studies conducted by Klein et al.[33] Dyslipidemia (elevated TC, TG & LDL and reduced HDL) was seen more in current smokers compared to ex-smokers and non-smokers and the difference was found to be statistically significant. This finding was comparable to studies done by Dawder TR et al,[34] Gofman JW et al.[35] Among the study group, dyslipidemia was found in > $9/10^{th}$ of patients. Impaired TC / HDL ratio is seen more commonly in current smokers than in non-smokers. The difference was statistically significant. These study findings were similar to studies done earliar by Fujiwara et al,[36] Steenkamp et al.[37] Total Cholesterol / HDL ratio was higher in patients with obstructive CAD as compared to those with normal angiogram, which was statistically significant. Roxana Campisi et al[38] showed smoking and, to a lesser degree, reduced HDL, increased LDL, increased total cholesterol / HDL ratio predict abnormalities in the myocardial blood flow response to cold, suggesting adefect located at the level of the coronary endothelium the severity of endothelial dysfunction is correlated with the duration of smoking. The abnormalities in coronary function as detected by quantitative PET imaging might represent an early stage of coronary artery disease in long-term smokers.

Smoking is associated with a direct toxic effect on human endothelial cells, reduces endothelial prostacyclin production, and increases leukocyte adhesion to endothelial cells, which is an early event in the atherosclerotic process. Cigarette smoke contains a large number of oxidants, and recent observations described a role of oxygen-derived free radicals in mediating endothelial dysfunction, which can be modulated by the potent antioxidant vitamin C. Alternatively, smoking increases endothelial angiotensin II production, which reduces nitric oxide activity that might contribute to endothelial dysfunction in smokers. Increased platelet aggregation and serum fibrinogen, as well as decreased serum plasminogen levels known to occur in smokers, might also impair endothelial function in smokers. Higher troponin I elevation was found in current smokers compared to non-smokers and ex-smokers indicating that more severe lesions and more extensive area of involvement. More the area of myocardial damage more will be the troponin elevation. Current smoker group had a greater number of patients with low ejection fraction as compared to non-smoker group. The sum of ST segment deviation or maximum ST segment deviation was significantly larger in current smokers than in non-smokers and ex-smokers. Patients with more ST segment deviation were found to have low ejection fraction. Angiographic evaluation showed more extensive CAD in smoker group as compared to non-smoker. TVD and DVD are more commonly seen in smokers. Greater ST segment deviation was found to be associated with more critical coronary artery disease. A study done by Stone PH.[39] reported that patients with Bundle branch block (BBB) had greater mortality, comparable to that in studies by Thompson B et al, the difference was statistically significant. LV dysfunction was more common in current-smokers and was lowest in non-smokers, indicating more severe disease in current smokers. Almost all the deaths occurred in patients with LV dysfunction, indicating its prognostic significance. This is similar to studies conducted by Khot UN et al and Klien et al[33] which showed that LV dysfunction in following myocardial infarction due to multivessel disease with critical lesions were more frequently seen in smokers as compared to non-smokers. Increased LDL was associated with increased mortality. It was more common in current smokers and it was found to be statistically more significant. This is similar to studies conducted by Isser et al, [40] whichshowed that smoking, high lipoprotein (a) and triglyceride levels and low high-density lipoprotein levels may be important risk factors for coronary artery disease in the younger population. Similarly, data were reported by Homer D et al,[41] Salonen JT et al.[42] Highest mortality was seen in current smokers. It may be related to increased dyslipidemia, severe disease as indicated by more extensive involvement and angiographically demonstrable occlusive disease and increased incidence of LV dysfunction. The data was found to be statistically significant. This is similar to the study conducted by Klein et al.[33]

CONCLUSIONS:

As age increases, incidence of ACS increases. Incidence of ACS is more in current smokers than in non-smokers. Sedentary physical activity is a risk factor for ACS. Dyslipidemia (elevated total cholesterol, triglyceride &LDL and decreased HDL) and impaired total cholesterol/HDL ratio is more commonly seen in current smokers than in non-smokers. NSTEMI is more common in non-smokers and STEMI is more common in current smokers. More ST deviation and Troponin I elevation is seen in current smokers. Patients with Bundle branch block, greater mortality. Non-smokers had milder disease on coronary angiography than ex-smokers and current smokers. LV dysfunction and triple vessel disease were more commonly seen in current smokers than ex-smokers & non-smokers and this was associated with increased mortality. Elevated LDL is associated with increased mortality. Thus, smoking in young adults has direct impact on the lipid profiles and morbidity and mortality of ACS. Smoking is a major risk factor for dyslipidemia and coronary artery disease. Mortality and morbidity in young patients are seen to be directly related to age, smoking, total cholesterol, LDL levels, total cholesterol/ HDL ratio, amount of troponin elevation, STEMI, conduction defect, amount of ST segment deviation, and extent of coronary artery disease lesions. It is inversely related to physical activity, HDL cholesterol levels and Ejection fraction. As it is a modifiable risk factor, the cessation of use of smoking and tobacco products, can cause considerable decrease in the morbidity and mortality.

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