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# Effects of Smoking on Lipid Profile and Homocysteine in Coronary Heart Disease

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**Abstract**

Smoking produces adverse effects on lipid profile and homocysteine, thus increasing the cardiovascular disease risk in coronary heart disease patients**.** The present study was undertaken to evaluate plasma lipid profile, lipoprotein (a) and homocysteine in coronary heart disease of smoker male and female patients in two age groups; below and above 50 years old, comparing them with nonsmokers healthy matched control. Triglyceride plasma level **(**291.33 ±101 mg/dl , mean ± SD, *P* value=0.01 ) was elevated significantly in smoking coronary heart disease males less than 50 years old as compared to controls, while cholesterol (233.54 ±44.9 mg/dl, *P* value= 0.02 ), LDL- cholesterol (174 ±58.3 mg/dl, *P* value=0.09 ) , lipoprotein (a) - Lp(a) (65.06 ±25.2 mg/dl, *P* value=0.05 ), and triglycerides (188.18 ±62.0 mg/dl, *P* value=0.01 ) are significantly increased in males more than 50 years old. No lipid profile parameter was significantly elevated in smoking coronary heart disease female less than 50 years old, while only homocysteine (28.83 ±5.7 mg/dl, *P* value= 0.02 ) was elevated significantly in females more than 50 years . In conclusion, smoking affects lipid profile and homocysteine and increases the cardiovascular disease risk among smokers.

**Keywords**: Cholesterol ,Low Density Lipoprotein Cholesterol, High Density Lipoprotein Cholesterol, Triglycerides, Homocysteine.

## 1. Introduction

As reported by different research groups, smoking increases the concentration of serum total cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol and decreases the levels of antiatherogenic HDL cholesterol (Adam *et al*., 2011; Austin, 1991; John and Rajat, 2004; Kavita *et al*., 2013; Muscat *et al.,* 1991). Smoking, in different forms, is a major risk factor for atherosclerosis and coronary heart disease (Fagerström, 2002; Vlassis, 2009). Passive smoking could affect blood lipid metabolism in women, which might contribute to coronary heart diseases (He *et al.,* 2007). A positive association between elevated plasma total homocysteine levels and a number of cardiovascular risk factors, smoking, particularly, was shown, in a study conducted in Norway (Wilcken, 2002), to be well associated. In the comprehensive analysis, now reported from the large European Concerted Action Project case control study, Callaghan and colleagues provide convincing evidence for an amplifying effect of cigarette-smoking on homocysteine associated cardiovascular risk (Callaghan *et al.,* 2002). Smokers (male and female) had significantly lower high-density lipoprotein levels and significantly higher very low-density lipoprotein total cholesterol and plasma triglyceride levels than nonsmokers (Meenkshisundaraum *et al*., 2010). The aim of the study is to find out the effect of smoking on serum lipid profile and homocysteine in coronary heart diseases in male and female patients of more and less than 50 years old. It also aims at assessing the association between smoking and the alteration in plasma concentration of lipid profile and lipid peroxides

## 2. Materials and Methods

A total number of 180 subjects were studied. Ninety were adult patients (of both sexes) with coronary heart diseases; they were admitted at coronary care unit in

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Princess Basma Teaching Hospital in Irbid City, the other 90 were age, and gender matched controls that referred to the lab of Princess Basma Teaching Hospital in Irbid City. All subjects did not suffer from obesity or blood pressure. Venous blood samples were collected after 12 hours of an overnight fast into plain and EDTA tubes. Serum or plasma was obtained by low speed centrifugation at 1000g for 15 minute, and samples were immediately separated into aliquot and stored at –20o C until analysis. The subjects were interviewed and a paper questionnaire and consent were completed, which included gender, age, smoking, DM, hypertension, type of CHD, previous history of CHD, and family history of CHD. Lp(a) was quantitatively estimated in serum by enzymatic immunosorbent assay (ELISA). IMMUN-OZYM Lp(a) kit manufactured by Progen, GMBH, Germany. Homocysteine (Hcy) in blood was quantitatively estimated in plasma by enzymatic immunosorbant assay (ELISA). Homocysteine Micro-plate Enzyme immunoassay kit manufactured by BIO-RAD, USA. Cholesterol, Triglyceride, and High-density lipoprotein/Low density lipoprotein were quantitatively estimated in the serum by enzymatic colorimetric test-CHOD-PAP by commercially available kits made by ARCOMEX, Jordan. Data are expressed as means and standard deviation (SD); means of the two groups were compared by student's t test. One-way analysis of variance test was used for comparison between more than two groups. Spearman's correlation was used to determine whether there was a relationship between Lp(a) and other variables. These statistical tests were performed using the Statistical Package for the Social Science (SPSS). The level of significance was $P<0.05$.

## 3. Results

Cholesterol (230.93±48.3 mg/dl, *P* value= 0.011), LDL-cholesterol (126.96±65.2 mg/dl, mean ± SD, *P* value=0.003 ), triglycerides (183.85±70.4 mg/dl, *P* value=0.00 ), and homocysteine( 24.35 ±11.6 mg/dl, *P* value=0.009 ) plasma levels significantly increased in coronary heart disease smokers (males and females less and more than 50 years old), while HDL- cholesterol (57.48 ±24.4 mg/dl, *P* value=0.027 ) significantly decreased as compared to control (Table 1). As shown in Table 2 only triglycerides (205.28 ±108.14 mg/dl, *P* value=0.025 ) significantly increased in smoking males and females coronary heart disease patients less than 50 years old. Plasma level of cholesterol (232.5 ±46.7 mg/dl, *P* value=0.02 ), LDL- cholesterol (184.20 ±67.9 mg/dl) (*P* value= 0,003), Lipoprotein (a) (60.22 ±24.6 mg/dl, *P* value=0.03 ), triglycerides (179.17 ±60.8 mg/dl, *P* value=0.00 ), and homocysteine (29 ±9.9 mg/dl, *P* value=0.00) significantly increased in smoking males and females coronary heart disease patients more than 50 years old, while HDL-cholesterol (55.83 ±24.1 mg/dl, *P* value=0.03) significantly decreased as compared to matched controls (Table 3). Cholesterol (233.3 ±43.3 mg/dl, *P* value=0.01 ), LDL-cholesterol (172.3 ±58.7 mg/dl, *P* value=0.00 ), triglycerides (198.86 ±72 mg/dl, *P* value=0.00 ) significantly increased and HDL- cholesterol (56.84 ±24.7 mg/dl, *P* value=0.00 ) significantly decreased in coronary heart disease male smokers (less and more than 50 years old) as compared to the matched control, while in females only homocysteine (26.4 ±5.8 mg/dl, *P* value=0.05 ) increased significantly (Table 4). As shown in table 5, only triglycerides (291.33 ±101 mg/dl, *P* value= 0.01) significantly increased in smoker coronary heart disease males less than 50 years old. Cholesterol (233.54 ±44.9 mg/dl, *P* value=0.02), Lipoprotein (a) (65.06 ±25.2 mg/dl), triglycerides (188.18 ±62.0 mg/dl, *P* value=0.01 ), LDL- cholesterol (174 ±58.3 mg/dl, *P* value=0.09) significantly increased in smoking coronary heart disease males more than 50 years old, while homocysteine (28.83 ±5.7 mg/dl, *P* value=0.02 ) significantly increased in females as compared to control (Table 6).

**Table 1.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker CHD and control mixed males and females more and less 50 years old

| Parameter ±SD | Non CHD | CHD | *P* |
|---|---|---|---|
| CHL(mg/dl) | 200.2 ±40.5 | 230.93 ±48.3 | 0.011 |
| LDL-CHL(mg/dl) | 129.8 ±68.2 | 126.96 ±65.2 | 0.003 |
| Lp(a) (mg/dl) | 39.5 ±18.4 | 53.9 ±24.4 | 0.102 |
| TG(mg/dl) | 114.2 ±51.1 | 183.85 ±70.4 | 0.00 |
| HDL-CHL(mg/dl) | 83.65 ±51.5 | 57.48 ±24.4 | 0.027 |
| Hmcy(mg/dl) | 14.84 ±6.9 | 24.35 ±11.6 | 0.009 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein; Lp(a): lipoprotein(a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine

**Table 2.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker mixed males and females CHD and controls <50 years old.

| Parameter ±SD | Non CHD | CHD | *P* |
|---|---|---|---|
| CHL(mg/dl) | 205.2 ±43.3 | 223.57 ±58.4 | 0.446 |
| LDL-CHL(mg/dl) | 122.1 ±52.2 | 154.43 ±48.0 | 0.199 |
| Lp(a) (mg/dl) | 24.8 ±6.5 | 32.5 ±8.7 | 0.18 |
| TG(mg/dl) | 111.8 ±60.06 | 205.28 ±108.14 | 0.025 |
| HDL-CHL(mg/dl) | 82.19 ±39.0 | 65.03 ±26.05 | 0.317 |
| Hmcy(mg/dl) | 7.62 ±4.1 | 15.06 ±9.7 | 0.20 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein;LP (a): lipoprotein (a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine.

**Table 3.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker mixed males and females CHD and controls >50 years old.

| Parameter ±SD | Non CHD | CHD | *P* |
|---|---|---|---|
| CHL(mg/dl) | 195.6 ±38.5 | 232.5 ±46.7 | 0.02 |
| LDL-CHL(mg/dl) | 131.2 ±82.3 | 184.20 ±67.9 | 0.03 |
| Lp(a) (mg/dl) | 43.09 ±21.2 | 60.22 ±24.6 | 0.03 |
| TG(mg/dl) | 116.9 ±43.4 | 179.17 ±60.8 | 0.00 |
| HDL-CHL(mg/dl) | 83.85 ±62.4 | 55.83 ±24.1 | 0.03 |
| Hmcy(mg/dl) | 17.25 ±5.9 | 29 ±9.9 | 0.00 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein; Lp(a): lipoprotein(a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine.

**Table 4.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker CHD and control males and females of mixed ages more and less 50 years old .

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| Parameter ±SD | Non CHD | CHD | P | Non CHD | CHD | *P* |
| CHL (mg/dl) | 193.6 ± 40.5 | 233.3 ± 43.3 | 0.01 | 212 ± 40.1 | 224.0 ± 62.6 | 0.63 |
| LDL-CHL (mg/dl) | 115.03 ±51.4 | 172.3 ± 58.7 | 0.00 | 147.9 ± 90.7 | 197.84 ± 82.2 | 0.22 |
| Lp(a) (mg/dl) | 39.61 ± 17.9 | 61.3 ± 20.5 | 0.57 | 39.38 ± 24 | 47.15 ± 44.6 | 0.45 |
| TG (mg/dl) | 114.78 ±54.8 | 198.86 ±72 | 0.00 | 113.19 ± 74.8 | 140.3 ± 24.4 | 0.21 |
| HDL-CHL (mg/dl) | 84.02 ± 35.3 | 56.84 ± 24.7 | 0.00 | 81.3 ± 6.8 | 59.33 ± 8.2 | 0.39 |
| Hmcy (mg/dl) | 12.50 ± 6.3 | 22.5 ± 14.3 | 0.07 | 17.85 ± 11.9 | 26.4 ± 5.8 | 0.05 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein; Lp(a): lipoprotein(a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine.

## 4. Discussion

The data show that only plasma level of triglycerides increased significantly in CHD smoking mixed population of males and females who were less than 50 years old, while all other lipid parameters increased, and HDL decreased in patients who were above 50 years old.

**Table 5.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker males and females CHD and controls <50 years old

| | Male | | | Female | | |
|---|---|---|---|---|---|---|
| Parameter ±SD | Non CHD | CHD | *P* | Non CHD | CHD | *P* |
| CHL (mg/dl) | 197.7 ± 44.9 | 231.34 ±33.6 | 0.26 | 228 ± 35.6 | 217.7 ±77.2 | 0.84 |
| LDL-CHL (mg/dl) | 103.36 ±40.6 | 157.67 ±72.1 | 0.12 | 178.3 ±47.7 | 152 ± 32.3 | 0.42 |
| Lp(a) (mg/dl) | 24.9 ± 8.0 | 31.5 ±9.4 | 0.36 | 25.6 ± 8.0 | 37 ± 25.4 | 0.10 |
| TG (mg/dl) | 108.82 ±63 | 291.33 ±101 | 0.01 | 118.3 ±62.1 | 140.7 ±59.1 | 0.65 |
| HDL-CHL(mg/dl) | 93.54 ±36.6 | 66.4 ±24.2 | 0.28 | 48.4 ±26.8 | 64 ±25.5 | 0.46 |
| Hmcy (mg/dl) | 6.16 ± 3.6 | 15.87 ± 11 | 0.21 | 12 | 11 | 0.99 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein; Lp(a): lipoprotein(a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine.

**Table 6.** Mean values and standard deviation of dyslipidemia indicators and homocysteine in smoker males and females CHD and controls >50 years old.

| | Male | | | Female | | |
|---|---|---|---|---|---|---|
| Parameter ±SD | Non CHD | CHD | P | Non CHD | CHD | *P* |
| CHL(mg/dl) | 188.47 ±36.8 | 233.54 ±44.9 | 0.02 | 204.05 ±42.8 | 228.2 ±58 | 0.43 |
| LDL-CHL(mg/dl) | 130.03 ±63.4 | 174 ±58.3 | 0.09 | 132.69 ±106 | 228.4 ±93 | 0.13 |
| Lp(a) (mg/dl) | 41.8 ±17.2 | 65.06 ±25.2 | 0.05 | 47.08 ±26.3 | 63.58 ±13.1 | 0.43 |
| TG(mg/dl) | 122.45 ±45.7 | 188.18 ±62.0 | 0.01 | 110.64 ±44.2 | 140.1 ±37.9 | 0.24 |
| HDL-CHL(mg/dl) | 71.77 ±32.0 | 55.74 ±77.2 | 0.16 | 97.5 ±87.2 | 56.21 ±25.6 | 0.28 |
| Hmcy(mg/dl) | 15.66 ±4.8 | 29.25 ±15.4 | 0.87 | 18.83 ±6.9 | 28.83 ±5.7 | 0.02 |

CHD: coronary heart disease, LDL-CHL: low density lipoprotein; Lp(a): lipoprotein(a); TG: triglyceride; HDL-CHL: high density lipoprotein; Hmcy: homocysteine

This finding may explain why all parameters increased ($p$<0.05) in mixed ages in those patients. Lipoprotein (a) increased but not remarkably, while homocysteine got significantly elevated. It could be concluded that the effect of smoking on the level of lipoprotein (a) is moderate while its effect on homocysteine is strong.

Smoking increased only the plasma level of triglycerides in CHD males whose age was less than 50 years, while it increased significantly the levels of cholesterol, lipoprotein (a), and triglcerides in CHD male patients above 50 years old. On the other hand, smoking had no effect on any lipid parameters in CHD female patients less than 50 years old, and only had a significant effect on increasing the homocysteine level in female patients more than 50 years old. It was observed that smoking affects lipid parameter in males more than 50 years old, while it affected homocysteine levels in females who were above 50 years old, and had no effect on lipoprotein (a) level in CHD males and females of different age groups. This sex role is due to the differences in the type and the dose of hormones between sexes. Estrogen has beneficial effects on cardiovascular health. A recent study suggested that estrogen may exert these effects by regulating the activity of liver enzymes involved in cholesterol metabolism (Szafran and Smielak-Korombel, 1998).

In general, smoking increased many lipid parameters and decreased the HDL plasma levels in CHD patients when compared to the control group. At the same time the level of homocystein also increased in those patients. It seems that an increase in both the homocystein and lipid profiles amplifies the risk factors toward cardiovascular diseases; this is in agreement with the findings reported by O'Callaghan and colleagues (Callaghan *et al*., 2002). A positive association is observed between elevated plasma total homocysteine and a number of cardiovascular risk factors including, smoking as reported by Nygard *et al.* (1995). This is in agreement with our results. Callaghan *et al.* showed that cardiovascular risk in smokers was markedly increased when plasma homocysteine also increased. Smokers with plasma homocysteine levels more 12 µmol./l had, a 12-fold increase of cardiovascular risk when compared with the risk in non-smokers with plasma homocysteine less than 12 µmol./l. A recent evidence for an association between elevated homocysteine and enhanced oxidative stress was shown by Yamamoto *et al.* (2000). Since it is now well established that cigarette smoking is also associated with an increase in markers of oxidative stress .Oxidative effects via free radical generation in smokers have been widely investigated. Oxidative stress causes lipid peroxidation, oxidation of proteins and damage to mainly tissues (Ozguner *et al*., 2005). Amplification by smoking of this homocysteine-related effect may be a mechanism contributing to the findings by O'Callaghan and colleagues of synergism between the two factors .Our results showed an increase in lipoprotein (a) plasma level in CHD patients who were more than 50 years old and specifically in males as a direct role of sex hormones (Szafran and Smielak-Korombel, 1998). This result is in agreement with what Barbagallo *et al.* reported in 1992. The increase in apolipoprotein (a) level could be due to oxidation or/and inhibition processes caused by smoking.

In conclusion, smoking produces adverse effects on lipid profile and homocysteine, thus increasing the cardiovascular disease risk. Further studies are needed to establish that smoking-related alterations have influences on the atherosclerotic lesions of smokers.

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