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Research Article

DETERMINATION OF INSULIN RESISTANCE IN YOUNG ADULTS AND ITS RELATION TO SMOKING

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ABSTRACT

Smoking is a major risk factor for diabetes mellitus, mainly due to decreased insulin secretion and increased insulin resistance (IR). The various complications associated with IR are cardiovascular disease (CVD), metabolic syndrome (MetS), diabetes, stroke and endothelial dysfunction. The IR prevalence in young adults and its relation to smoking is not clearly demonstrated. So, this study was planned to estimate the effects of smoking on IR. This study comprised 40 young adults who smoked minimum 6 beedis/cigarettes daily and 25 age matched control subjects. Blood samples were collected in plain bulb and biochemical analyses like fasting blood glucose (FBG), lipid profile, fasting insulin were done and then Homeostatic Model Assessment of Insulin Resistance was used to find out IR. Smokers has significantly higher level of fasting blood glucose, fasting insulin, total cholesterol, triglycerides, LDL-C, HOMA-IR index and lower level of HDL-C as compared to non-smokers. A significant association was noted between the smoking status, including both the numbers of cigarettes/beedis smoke per day and fasting insulin level as well as for HOMA-IR index. Smokers have a high risk of developing an insulin resistance and hyperinsulinemia as compared with a matched group of non-smokers. This may help to explain the high risk of cardiovascular disease in smokers.

Keywords: Insulin Resistance, Cardiovascular disease, Metabolic Syndrome, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), Smoking

1. INTRODUCTION

Smoking is the major global cause of preventable death. The most popular form of smoking is tobacco smoking and is practiced by over one billion people in the majority of all human societies [1]. Smoking is one of the modifiable risk factors for many chronic diseases, such as cancer, chronic obstructive lung disease, asthma, atherosclerosis, coronary heart disease and peripheral vascular disorders. Smoking also increases inflammation and oxidative stress to directly damage β (Beta) cell function and to impair endothelial function [2]. Long-term smoking is reported to increase insulin resistance (IR), inflammation, lipid peroxidation and endothelial cell dysfunction [3].

In India, 337 million people above 10 years of age consume tobacco. Many people are active or passive smokers including 1.1 Billion smokers, which is approximately one third of the adult population [4]. The World Health Organization (WHO) predicts that tobacco deaths in India may exceed 1.5 million annually by 2020 [5]. In 2000, 1.69 Million resident's world-wide dead of coronary heart disease (CHD) or cardiovascular disease (CVD) caused by smoking [6]. By 2020, smoking will cause 8.4 Million deaths and will be the largest health problem. The leading causes of deaths from smoking are cardiovascular disease (1.69 Million deaths), chronic obstructive pulmonary disease (0.97 Million deaths) and lung cancer (0.85 Million deaths). Tobacco use accounts for one in 10 adult deaths, nearly one person die every six seconds.

Nicotine (Ni) in smoking person can make the blood sugar level go up or down. The chemicals alter the way that our body can use glucose. It changes chemical process in our body cells like inflammation, tissue damage and vascular effect. So, they don't respond to insulin and let in, the condition develops where insulin resisted by cells called IR. Smoking also causes molecular changes in lipid metabolism and glucose metabolism [7].

In healthy young men, acute smoking showed an increased IR [8]. IR is considered to be primary initiating

factor for obesity, type 2 diabetes mellitus (T2DM or T2D), dyslipidemia and cardiovascular disease in adults. IR is known to be associated with abnormal lipid profile in obese children, adolescents and adults [9]. There is increasing evidence that prevalence of IR is increasing in childhood and adolescence [10]. Interestingly IR has also been reported in Lean Asian population as well as normal body weight subjects, with greater whole-body fat and higher levels of muscle lipids. However, the mechanism which contributes to the impaired insulin signaling in the absence of obesity is not much clear. Although smoking is known to decreases body weight, it is associated with central obesity [11]. Furthermore, few studies have demonstrated that smoking cessation is associated with improvement in insulin sensitivity. Stopping smoking at age 60, 50, 40, or 30 years leads to a gain of about 3, 6 and 9 or 10 years on life expectancy according to the study among male British doctors followed -up for 50 years. High Insulin concentrations and different degrees of insulin resistance have been found in smokers and in contrast, smoking cessation would significantly increase the Insulin Sensitivity.

Homeostatic model assessment of insulin resistance (HOMA-IR) has been found to be a convenient and reliable method for evaluating IR. It is considered as a better marker than plasma insulin levels and compares well with IR measured by euglycemic clamp method. Ikedy et al. reported that HOMA-IR is better, inversely correlated to glucose infusion rate than fasting plasma insulin levels, in both diabetic and non-diabetic patients [12]. Many studies have shown increased IR in people leading sedentary lifestyle and consuming high-fat diet. However, the status of IR in young Indian, who is obese and has smoking habit corollary, is yet not plenty known [10, 13]. So, the main aim of the present study was to determine the IR in young adults and its relation to smoking.

2. MATERIAL AND METHOD

2.1. Population

This cross-sectional study included 40 young adults (mean age: 37.6±4.2 year) who smokes daily 6 cigarettes/ beedis and 25 (mean age: 35.2±4.3 year) age matched non-smokers. Written informed consent was obtained from all voluntary adult participants. Ethical clearance was taken from the institutional human research ethics committee to perform this study.

2.2. Smoking questionnaire

Smoker's information and cigarette smoking outcome data were collected at consenting time. The majority of current and former smokers were able to provide information on the number of cigarettes they smoked and duration of smoking. Smokers were questioned about their age, gender and history problems if any.

2.3. Sample collection

Fasting venous blood of patients and control group was collected in fluoride bulb and plain bulb. Then the samples were centrifuged at 3000 rpm for 10 minutes to separate plasma and serum for further biochemical analysis.

2.4. Laboratory analysis

All the samples were tested for Fasting Blood Glucose (GOD/POD method) [14], TG (GPO/PAP method) [14, 15], Total Cholesterol (HOD/POD method) [14, 16], LDL-C and HDL-C (Direct enzymatic method) [14, 17] by using automated biochemistry analyzer. For quantitative determination of fasting insulin, we used ADVIA Centaur CP Insulin (IRI) Assay, a two-site sandwich immunoassay using direct chemiluminescent technology [18].

2.5. Data measures

Insulin Resistance was calculated using HOMA-IR model equation [18]:

HOMA-IR = FBG (mmol/L) × Fasting Insulin (mIU/ml)/22.5

Values above 2.5 were taken as abnormal and reflect the insulin resistance.

2.6. Statistical analysis

Statistical analysis was performed using the SPSS software (version 15.0). Quanititative variables were presented as mean ± S.D. and comparisons were performed using Students's *t*-test (unpaired student's *t* test) [19]. Statistical significance was considered when $P < 0.05$.

3. RESULTS

The study describes HOMA-IR in young adults in relation to smoking habits. A total of 40 young adults were screened who smoked and 25 young adults who never smoked.

Table 1 show that the mean age of smokers was 37.6±4.2 years and for non-smokers it was 35.2±4.3 years.

Table: 1 Age wise distribution

Group	Smokers (n=40)	Non-smokers (n=25)
Age in years	37.6 ± 4.2	35.2 ± 4.3
Male	40 (62.5 %)	25 (37.5 %)

Table: 2 BMI, FBS and Fasting Insulin in Smokers and Non-Smoker

Group	Smokers	Non-smokers	p-value
BMI (kg/m^2) Mean±SD	29.31±5.37	25.06±4.13	0.025
FBS (mg/dl) Mean±SD	99.97±16.87	85.94±10.38	0.000
F. Insulin (mIU/dl) Mean±SD	15.35±5.29	12.32 ±2.14	0.003

The levels of FBS and F. Insulin were increased moderately to severely in smokers as compared to non-smokers as shown in above table 2. The mean BMI was 29.3±4.57 kg/m^2 in smokers and 25.18±1.13 kg/m^2 in non-smokers. It was significantly higher in smokers than non smoker ($p < 0.025$). The FBS level was significantly increased in smokers as compared to non-smokers [p-value= 0.00 ($p < 0.05$)]. F. Insulin level was significantly higher among smokers than non-smokers [p-value= 0.003 ($p< 0.05$)].

Table: 3 HOMA-IR Index between smokers and non-smokers

Group	Smokers	Non-smokers (Control)	p-value
HOMA-IR Mean±SD	3.72±1.16	2.61±0.51	0.000

Insulin resistance was calculated by using the formula (HOMA-IR=FBG (mmol/L) × F. Insulin (mIU/ml) / 22.5.

HOMA-IR Index in the smokers was 3.72±1.16 and 2.61 ± 0.51 in non-smokers. HOMA-IR was increased moderately to severely in smokers as compared to non-smokers as shown in above table 3.

Table: 4 Comparison of Lipid Profile between Smokers and Non-smokers

Group	Smokers	Non-smokers (Control)	p-value
Cholesterol (mg/dl) Mean± SD	192.47±40.13	173.88±32.12	0.012
TG (mg/dl) Mean±SD	168.65±127.91	111.60±33.62	0.013
LDL-C (mg/dl) Mean±SD	120.52±38.31	87.44±13.23	0.000
HDL-C (mg/dl) Mean±SD	43.85±12.37	50.82±10.43	0.024

The table 4 compares the lipid profile between smokers and non-smokers and shows a significant increase in Cholesterol, TG and LDL-C levels and decreased in HDL-C (good cholesterol) level in smokers as compared to non-smokers ($p< 0.05$).

4. DISCUSSION

Insulin Resistance is main factor in the pathophysiology of metabolic syndrome. Further, IR is linked with sedentary life style, high-fat diet and smoking. Some studies have suggested that smoking impairs glucose tolerance and insulin sensitivity. The risk for IR is also closely linked to degree of smoking [20]. Raised HOMA-IR and TG in smokers can be due to nicotine content of cigarette/beedi. Later due to IR the various pathophysiology of metabolic syndrome develops and it may result in weight gain. [8, 21, 22]. Eliasson et al. have reported that smokers display typical features of the so-called IR syndrome, and that the degree of IR and extent of related metabolic abnormalities are strongly associated with smoking habits [23].

Our data in this study showed that smokers had significant higher levels of fasting glucose, fasting insulin, lipid profile and HOMA-IR index in smokers. Similar study carried by Gupta et al. reported statistically significant increased fasting insulin in smokers [24]. The possible result may be due to the chemicals contents in cigarette/beedis changes chemical process in our body which leads to resists the response of insulin activity of insulin hormone by cells or tissues [7].

Will et al. in 2001 found that stopping smoking can reduce the risk of diabetes to that of non-smokers after 5 years in women and after 10 years in men [25]. This

suggests that the smoking-related risk of diabetes is reversible in those who leave the habit. Quitting smoking can also reduce the risk of death in diabetic patients who smoke, although the risk of mortality is correlated with the duration of the smoking habit, highlighting the importance of addressing the issue of smoking in all patients with diabetes.

In the current study we observed altered lipid profile in smokers. The study documented that there was significant increase in levels of total cholesterol, TG, LDL-C, VLDL-C in smokers than non-smokers. The total cholesterol level in smokers was significantly higher (i.e. 192.47±40.1 mg/dl) than in non-smokers which is correlated with the study done by Joshi et al. who reported increased total cholesterol level i.e. 159.2±29.5 mg/dl in smokers. They also postulated that increase in the total cholesterol level correspond ended with increase in number of cigarettes/beedis smoked [26]. In present study, TG, LDL-C levels were significantly high in smokers as compared with non-smokers. In contrast the level of HDL-C was significantly reduced in smokers. These results where analogous with the observations of Devaranvadgi BB et al. where TG level was 166.84±27 mg/dl, LDL-C level was 127.13±20.68 mg/dl in smokers and HDL level was 35.91±4.51 mg/dl in non-smokers [27]. The increased lipid profile in smokers may be due to decreased activity of lipoprotein lipase and hepatic lipase in smoking activity. Smoking impairs human serum Paraoxygenase activity and there by affect antioxidant defense mechanism.

The possible mechanism for dyslipidemic among smokers were following: (a) Nicotine stimulates the release of adrenaline from the adrenal cortex leading to increased serum secretion of cholesterol as well as hepatic secretion of very low-density lipoprotein (VLDL) and increased TG. (b) HDL concentration was inversely related to VLDL concentration in serum [28]. (c) Smoking increases IR and causes hyperinsulinemia, LDL, VLDL and TG are elevated in hyperinsulinemic conditions due to decreased activity of lipoprotein lipase and hepatic lipase has been activated, which converts VLDL to LDL [29]. Stopping of smoking has been shown to increase insulin sensitivity and improve the lipoprotein profile. Although smoking cessation has beneficial effects on CVD morbidity and mortality, it is also associated with weight gain, which is also a strong risk factor for CVD.

In the present study the mean HOM-IR was significantly higher in smokes than non-smokers. The determined HOM-IR mean was 3.72±1.16 in smokers, in non-smokers it was 2.61±0.51. Bajaj postulated that nicotine triggers IR in smokers [30]. Gupta et al. conducted a study on effect of cigarette smoking on IR in asymptomatic adults and reported statistically significant increased in serum insulin and HOMA-IR index in smokers [24]. Targher et al. reported a link between cigarette smoking and IR in T2DM and associated dyslipidemia [31]. A negative effect of cigarette smoking on insulin sensitivity has been documented in several studies [32]. Moreover, cigarette smoking may release oxygen-free radicals, which could reduce insulin sensitivity. Experimental findings suggest that smoking causes IR [30, 33]. Indeed, stopping smoking can increase life expectancy even in those who leave the habit after the age of 65 years. To reduce the burden of illness due to smoking, health professionals need to encourage stopping smoking [34].

5. CONCLUSION

Smokers have high level of fasting blood glucose, hyperinsulinemia, compared with matched group of non-smokers and may help to explain the high risk of cardiovascular disease in smokers. The HOMA-IR index was also significantly high in smokers as compared to non-smokers. Insulin plays an important role in maintaining the balance between nutrient demand and availability by integrated set of signals. Impaired nutrition due to smoking also contributes to hyperlipidemia and insulin resistance causing hyperglycemia. Smokers had dyslipidemia which may expose the vascular endothelium to potentially atherogenic lipoprotein which predisposes the greater risk of developing atherosclerotic plaque and cardiovascular disease. Smoking increases diabetic incidence by disturbing the glucose homeostasis, which later leads to chronic diabetic complications. The analysis informed that individual with HOMA-IR of > 3 value considers as more prone to develop IR, as seen in smokers. In contrast the HOMA-IR value < 3 may consider as less prone to develop IR as seen in non-smokers. The earliest intercession of smoking may cause favorable effects on lipid profile particularly with increased HDL-C. Stopping smoking can also cure the blood glucose level and activity of insulin hormone, which leads to prevent the fasting insulin increase in blood. Thus earliest cessation of smoking help to prevent future health hazards developed due to IR. Thus educating smokers and termination of smoking are important strategies for the management of smoking.

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