Insulin Resistance in Young Obese Subjects and Its Relation to Smoking (A Pilot Study)

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Abstract Insulin resistance is a condition in which cells fail to respond to the normal actions of insulin. Dietary fat, obesity and smoking have been attributed to increase insulin resistance. However, the prevalence of insulin resistance in young obese subjects and its relation to smoking is not well established. This study comprising seventy-five healthy young adults was undertaken to find insulin resistance in obese smokers and non smokers both. Present study showed an overall prevalence of raised homeostatic model assessment of insulin resistance in 14.7 % otherwise healthy young subjects (20–30 years age group). Non-smokers did not show any significant correlation between insulin resistance and body mass index at either stage (normal, pre-obese as well as obese). Smokers also did not show any significant difference of insulin resistance in normal and pre-obese stages. However, marked increase in homeostatic model assessment of insulin resistance was observed in obese smokers. Homeostatic model assessment of insulin resistance showed a linear trend in relation to body mass index and its values were found to be higher in smokers. Obesity combined with smoking demonstrated statistically significant increase in homeostatic model assessment of insulin resistance.

Keywords Cardiovascular disease (CVD) · Fasting blood glucose (FBG) · Homeostatic model assessment of insulin resistance (HOMA-IR) · Insulin resistance (IR) · Short term

studentship (STS) · Type 2 diabetes mellitus (T2DM) · Triglyceride (TG) · Jun amino-terminal kinases (JNK)

Introduction

Insulin resistance (IR) is considered to be primary initiating factor for obesity, diabetes mellitus, dyslipidemia and cardiovascular disease (CVD) in adults. It is known to be associated with abnormal lipid profiles in obese children, adolescents, and adults [1]. There is increasing evidence that prevalence of IR is increasing in childhood and adolescence [2]. 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 signalling in the absence of obesity is not much clear. Mashrani et al. [3] reported insulin resistance to be associated with activation of the JNK pathway in non-obese subjects. This issue remains controversial and additional studies are required, particularly among women.

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 insulin resistance measured by euglycaemic clamp method. Ikedy et al. [4] reported that HOMA-IR is better, inversely correlated to glucose infusion rate than fasting plasma insulin levels, in both diabetic and non-diabetic patients. HOMA-IR correlates more with visceral fat area than with subcutaneous fat area.

Many studies [2, 5] have shown increased insulin resistance in people leading sedentary lifestyle and consuming high-fat diet. However, the status of insulin

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resistance in young Indian, who are obese and have smoking habit concomitantly, is yet not amply known.

The present study was therefore undertaken in young Indian adults to understand the relation of body mass index (BMI), smoking habit, fasting blood glucose (FBG), high density lipoprotein- cholesterol (HDL-C) and triglyceride (TG) levels.

Materials and Methods

The study was carried out in 75, otherwise healthy, asymptomatic, young volunteers, either sex, in the age group of 20–30 years.

Inclusion Criteria

Non-Smokers—Healthy individuals (students/employees/attendants of the patient),

Smokers—Similar subjects with h/o smoking (minimum of 6 cigarettes, bidi/day).

Exclusion Criteria

Alcoholics and drug addicts were excluded from the study.

The study groups

A) 25 smokers (all males). B) Non-smokers—50 (24 males, 26 females).

The subjects were divided according to their BMI (kg/m^2), as per ICMR guidelines (Table 1) Mishra et al. [5].

Table 1 Break up of subjects according to their BMI (kg/m^2)

	Normal 18.1–22.9 n (%)	Over weight 23–25 n (%)	Obese >25 n (%)
Non-smokers (n = 50) Male: 24, female: 26	23 (46 %)	11 (22 %)	16 (32 %)
Smokers (n = 25) All males subjects	19 (76 %)	4 (16 %)	2 (8 %)
Total (n = 75)	42 (56 %)	15 (20 %)	18 (24 %)

Table 2 HOMA-IR Index
(Mean $\pm$ SD)

	Male	Female	(Male and female)	p value (male versus female)
HOMA-IR	1.71 $\pm$ 1.68 (n = 49)	1.82 $\pm$ 1.76 (n = 26)	1.75 $\pm$ 1.70 (n = 75)	>0.05
	A. Smokers only males	B. Non-smokers only males	C. Non-smokers (male and female)	A versus B and A versus C
HOMA-IR	1.75 $\pm$ 2.11 (n = 25)	1.66 $\pm$ 1.12 (n = 24)	1.74 $\pm$ 1.47 (n = 50)	>0.05

Biochemical Analysis

5 ml of venous blood was collected in the fasting state, taking all aseptic precautions. Serum insulin, fasting blood glucose (FBG), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) were analysed on fully automated biochemistry analyser.

Serum insulin was estimated by sandwich ELISA technique. Insulin resistance was calculated by the formula—[HOMA-IR = FBG (mmol/L) $\times$ FPI (mIU/ml)/22.5 [6].

Statistical Analysis

Data was expressed as group mean $\pm$ SD and analyzed by ‘unpaired *t* test’ in different BMI groups. *p* values <0.05 were considered statistically significant (Table 2).

Results and Discussion

Insulin resistance has been implicated in the etiology of diabetes mellitus, metabolic syndrome and related cardiovascular disorders. Further, IR is linked with sedentary life style, smoking and high-fat diet. Present study describes HOMA-IR in young, otherwise healthy Indian adults in relation to their BMI, smoking habits, FBG, TG and HDL-C (Table 3).

HOMA-IR in Young Indian Subjects

The difference in HOMA IR values between male and females; was statistically not significant, in confirmative with earlier report Hanley et al. [1].

Prevalence of Insulin Resistance in Young Indian Subjects [6]

85.3 % subjects showed mean HOMA-IR values, with in the normal range (<3.0), as reported in literature [6]. However, 14.7 % cases showed raised HOMA-IR levels. [8 % showing moderate increase (3–5) and 6.7 % showing severely increased HOMA IR level (>5.0)].

Table 3 Distribution of subjects according to HOMA-IR status

HOMA-IR range	Normal		Moderate increase		Severe increase	
	<3		3–5		>5	
	n	%	n	%	n	%
Female (F) (n = 26)	22	84.6	2	7.7	2	7.7
Male (M), (n = 49)	42	85.7	4	8.2	3	6.1
Total (F + M), (n = 75)	64	85.3	6	8	5	6.7

Fig. 1 HOMA-IR in relation to BMI (smokers and non-smokers combined) **Table 4** HOMA-IR in relation to BMI in smokers and non-smokers

Group	Smokers (males)		<i>p</i> val A versus C	Non-smokers (males)		<i>p</i> val. B versus D
	A. BMI	B. HOMA-IR		C. BMI	D. HOMA-IR	
Normal (BMI < 22.9 kg/m ²)	19.5 ± 1.88 (n = 19)	1.35 ± 6.59 (n = 19)	<0.05	21 ± 1.8 (n = 10)	1.64 ± 1.51 (n = 10)	>0.05
Over weight (BMI 23–25 kg/m ²)	24.3 ± 0.38 (n = 4)	1.49 ± 1.49 (n = 4)	>0.05	23.8 ± 0.35 (n = 4)	1.94 ± 0.91 (n = 4)	>0.05
<i>p</i> value Normal versus Ov. Wt	<0.001	>0.05		<0.05	>0.05	
Obese (BMI > 25 kg/m ²)	26.7 ± 1.2 (n = 2)	6.19 ± 2.39 (n = 2)	>0.05	27.7 ± 1.48 (n = 10)	1.56 ± 0.78 (n = 10)	<0.01
<i>p</i> value Over wt/Obese	<0.05	<0.05		<0.001	>0.05	

HOMA-IR in Relation to BMI

HOMA-IR showed linear increasing trend from normal to over-weight and obese groups (irrespective of smoking habit), however this difference was statistically insignificant (Fig. 1).

HOMA-IR in Relation to BMI and Smoking Habit (Table 4)

Smoking habit did not show any significant impact on HOMA-IR values in normal and overweight groups. However, obese smokers (BMI > 25 kg/m²) showed a significant, four-fold increase in HOMA-IR compared to obese non-smokers. In contrast, obese non-smokers also did not show any significant difference in HOMA-IR compared to normal and overweight groups. Thus, it can be inferred

that smoking assumes an important contributory role in the pathogenesis of insulin resistance in obese subjects.

Lipid Profile and Fasting Blood Glucose (FBG) in Smokers and Non-smokers

Total cholesterol value in smokers is higher than non-smokers ($p > 0.05$). Triglyceride and HDL-C values in smoker and non-smokers are not statistically significant. Joshi et al. conducted a similar study on the effect of smoking on lipid profile and reported, total cholesterol value increased in smokers. They also postulated that increase in the total cholesterol value corresponded with increase in number of cigarette/bidis smoked [7]. The difference of fasting blood glucose in smokers and non-smokers found not significant (Table 5).

Table 5 Lipid profile and Fasting blood glucose (FBG) in smokers and non-smokers

	T. Cholesterol (mean $\pm$ SD)	Triglyceride (mean $\pm$ SD)	HDL-C (mean $\pm$ SD)	FBG (mean $\pm$ SD)
Non-smokers (n = 50)	137.8 $\pm$ 26.29	92.06 $\pm$ 43.6	48.2 $\pm$ 9.6	91.9 $\pm$ 5.5
Smokers (n = 25)	159.2 $\pm$ 29.5	95.1 $\pm$ 45.9	44.04 $\pm$ 16.02	92.2 $\pm$ 5.12
<i>p</i> value	<0.05	>0.05	>0.05	>0.05

Smoking, Obesity and Insulin Resistance in Young Obese Subjects

In the present pilot study, non-smokers did not show significant correlation between HOMA-IR and BMI at either stage (normal, pre-obese as well as obese). Smokers also did not show any significant difference in HOMA-IR in normal and pre-obese stages. However marked increase in HOMA-IR was observed in smokers at the obese stage. This tallies well with clinical experience. Smokers who are obese often turn out to be diabetic and noted to have coronary artery disease. Gupta et al. [8] conducted a study on effect of cigarette smoking on insulin resistance in asymptomatic adults and reported statistically significant increase in serum insulin and HOMA-IR index in smokers, ($p < 0.001$). Suganthy et al. [9] conducted a similar study on obesity and insulin resistance among cigarette smokers and reported impaired insulin response in cigarette smokers.

Bajaj [10], postulated that nicotine triggers insulin resistance in smokers. Raised HOMA IR and TG in smokers can be attributed to nicotine content of cigarette/bidis. Similarly glucogenic response can also be attributed to nicotine induced increase in plasma cortisol levels.

It is postulated that smoking induced biochemical changes in subjects with obesity makes them vulnerable to insulin resistance and T2DM. Targher et al. [11] reported a link between cigarette smoking and insulin resistance in T2DM and associated dyslipidemia. These proatherogenic changes finally lead to metabolic syndrome and CAD. Thus quite understandably smoking by an obese individual can further induce insulin resistance leading on to associated metabolic disorders and CAD in future.

Conclusion

Based on this pilot study it may be said that young smokers with obesity are prone to develop insulin resistance. However, the effect of obesity and smoking on insulin resistance needs to be explored further on a larger sample size to conclusively elucidate their relationship.

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Compliance with Ethical Standards

Limitations Small sample size and lack of female smokers in our study are the constraints. It needs to be studied in larger sample size.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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