

## THE EFFECTS OF CIGARETTE SMOKING ON GLYCOSYLATED HEMOGLOBIN (Hb A1C) IN NON-DIABETIC INDIVIDUALS

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### ABSTRACT

**Background:** Cigarette smoking is associated with an increased risk of Type 2 diabetes mellitus. Glycosylated hemoglobin (Hb A1c) is a marker of long-term glucose homeostasis reflecting an average blood glucose concentration in past 2-3 months. The effect of cigarette smoking on average blood glucose levels as measured by glycosylated hemoglobin have yet received little attention. This study was done to assess the effect of smoking on blood glucose concentration by comparing glycosylated hemoglobin (Hb A1c) between non-diabetic cigarette smokers and non-smokers. **Materials and Methods:** This is a cross sectional case control study involving 60 participants with case group consists of 30 non-obese, non-diabetic males of age group between 20-40 years who smoke 10 filter cigarettes per day or more for not less than 5 years. 30 healthy age matched non-obese males who do not smoke cigarette were recruited for control group. After an overnight fast of 12 hours the serum glucose concentration and the glycosylated hemoglobin levels were estimated in all subjects and the values were compared between the cases and control using students 't' test. **Result:** There is no significant increase in the fasting serum glucose levels between the cases  $100.2 \pm 12.37$  and the controls  $103.1 \pm 9.64$ . There is a significant increase in the glycosylated hemoglobin level in smokers  $5.48 \pm 0.83$  when compared with the non-smokers  $4.56 \pm 0.34$  with  $p$ -value  $< 0.001$ . **Conclusion:** The results from the present study suggest that the level of glycosylated hemoglobin is increased in the non-diabetic smokers when compared to the non-smokers.

### INTRODUCTION

Cigarette smoking is known to cause a transient elevation of blood glucose concentration. The smokers display the typical features of the so-called insulin resistance syndrome and the extent of the related metabolic abnormalities are strongly associated with smoking habits. Nicotine, which is the most abundant volatile alkaloid in cigarette, has been demonstrated to increase the blood glucose levels. Many previous prospective studies had suggested that the cigarette smoking might be associated with the increased risk of type 2 diabetes mellitus in both men and women.<sup>[1-10]</sup>

Glycosylated hemoglobin (Hb A1c) is a marker of long-term glucose homeostasis reflecting the average blood glucose concentrations in past 2-3 months. Glycosylated hemoglobin (Hb A1c) is formed by non-enzymatic condensations of glucose with N-terminal valine residue of each  $\beta$  chain of Hb A. This glycosylated hemoglobin values are free from day to day blood glucose fluctuation and are

unaffected by exercise or recent food ingestion. Microvascular complications of diabetes are associated with the increase in the concentration of glycosylated hemoglobin (Hb A1c). It may also predict the cardiovascular disease.<sup>[5,11-15]</sup>

Investigating the association between smoking and glycosylated hemoglobin (Hb A1c) may clarify the role of smoking as a risk factor for diabetes and its complications. The effect of cigarette smoking on average blood glucose levels as measured by glycosylated hemoglobin have yet received little attention. Hence this study was taken to assess the effect of smoking on blood glucose level by comparing glycosylated hemoglobin levels between non-obese, non-diabetic smokers and non-smokers.<sup>[16-19]</sup>

### Aim and Objectives

The main aim of the study is to estimate the glycosylated hemoglobin (Hb A1c) levels in the non-diabetic cigarette smokers and the non-smokers and to compare the levels between the two groups to assess the effect of smoking on the glycosylated hemoglobin (Hb A1c).

## MATERIALS AND METHODS

This was a cross sectional case control study involving 60 participants. All the participants were selected randomly from the general population.

**Study population:** The study group comprised of 30 non-diabetic, non-obese males of age group between 20-40 years who smoke 10 filter cigarettes per day or more for not less than 5 years. 30 healthy age matched non-obese males who do not smoke cigarette were recruited in the control group. All subjects were from the similar socio economic status.

### Exclusion Criteria

Patients suffering from diabetes mellitus, hypertension, renal disease, hepatic disease, ischemic heart disease, hemoglobinopathies, anemia, acute or chronic blood loss, history of medications such as hormonal therapy, steroid therapy, anticonvulsant therapy and diuretic therapy were excluded from this study. Subjects with the history of alcoholism, history of other forms of tobacco intake and the smokers who smoke less than 10 cigarettes per day were also excluded from this study.

Family history of metabolic diseases including diabetes, hypertension and ischemic heart disease were obtained from all subjects. Written consent was obtained from subjects after their requirements for participation in the study were explained.

**Anthropometric measurements:** The height and weight of the subjects were measured by using

standard methodology with the help of inch tape and weighing machine and the Body Mass Index (BMI) was calculated by using Quetelet Index using the formula  $Wt(kg)/Ht(m^2)$ . Waist circumference was measured at the midpoint between the lower margin of the rib and the top of the iliac crest in cms and the hip circumference was measured around the widest portion of the buttocks in cm using non-stretchable inch tape. Waist-to-hip ratio (WHR) was calculated using these measurements

**Biochemical analysis:** After twelve hours of overnight fast, 3ml of blood samples were obtained from all the subjects by venipuncture from cubital fossa in sterile vacuum tubes using dispovan. Estimation of serum glucose was done by standard glucose oxidase, GOD/POD method (Beacon diagnostics pvt. Ltd., India). Glycosylated hemoglobin was measured by High performance liquid chromatography (HPLC) method using D-10 HbA1c kit (Bio-Rad laboratories, USA)

**Statistical analysis:** The values were expressed as mean  $\pm$  standard deviation. The data from the cases and control groups were compared by using Student's t-test using SPSS (Statistical Package for Social Science) software, version 3.5. P values  $<0.05$  were considered to indicate statistical significance.

## RESULTS

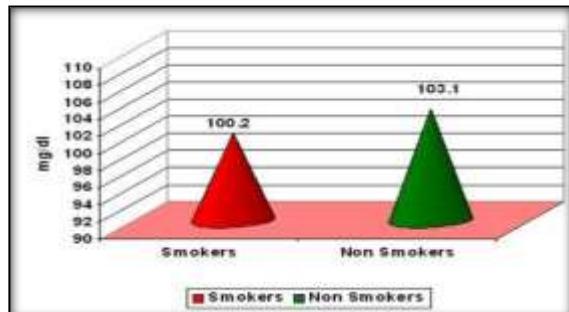
The findings of the current study are summarized in the table.

**Table 1: Observation of different parameters and its mean values between the smokers and non-smokers**

Variables	Smokers (n=30)	Non-smokers (n=30)	P value
Age (yrs)	28.96 $\pm$ 5.3	29.06 $\pm$ 4.47	0.937
Body Mass Index (BMI)	23.09 $\pm$ 3.11	23.45 $\pm$ 2.53	0.627
Waist-to-hip ratio (WHR)	0.84 $\pm$ 0.25	0.86 $\pm$ 0.22	0.734
Fasting serum glucose (mg/dl)	100.2 $\pm$ 7.52	103.1 $\pm$ 4.93	0.009
Glycosylated hemoglobin (HbA1c) (%)	5.48 $\pm$ 0.83	4.56 $\pm$ 0.34	<0.001

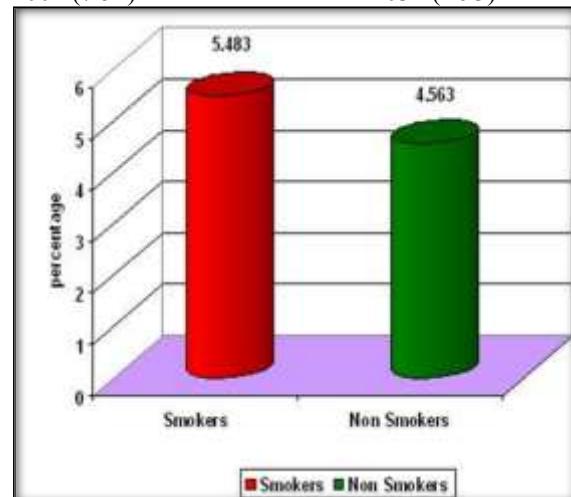
p-value  $< 0.05$  is significant.

The findings of the current study show that the mean age for case group is 28.96 (5.3) and that of control group is 29.06 (4.47). The mean BMI for the cases and controls are 23.09 (3.11) and 23.45(2.53) respectively. The mean Waist-to-hip ratio (WHR) of smokers and non-smokers are 0.84(0.25) and 0.86(0.22) respectively. There is no significant difference in BMI and Waist-to-hip ratio (WHR) between the smokers and non-smokers.



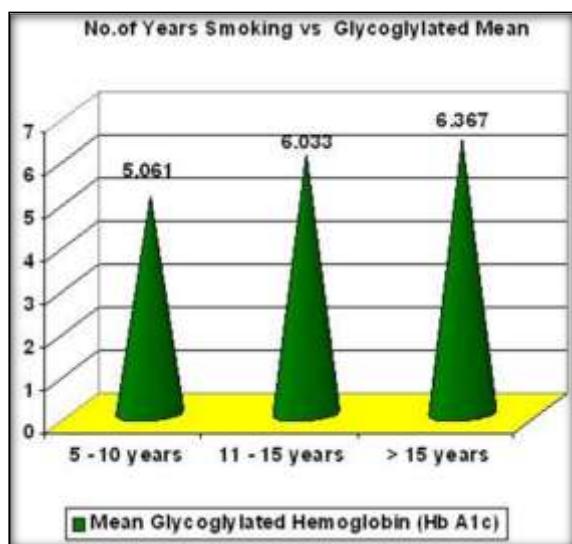
**Figure 1: Comparison of fasting serum glucose levels between the smokers and non-smokers**

There is no significant difference in the fasting serum glucose level between the smokers 100.2(7.52) and the non-smokers 103.1(4.93).



**Figure 2: Comparison of Glycosylated hemoglobin (HbA1c) between Smokers and non-smokers**

When the glycosylated hemoglobin levels are compared between the smokers and the non-smokers there is a significant difference with the smokers having higher HbA1c levels 5.48(0.83) when compared to non-smokers 4.56 (0.34).



**Figure 3: Comparison of years of smoking and the mean glycosylated hemoglobin (Hb A1c) in smokers**

When the smokers are grouped according to the number of years of smoking there is a linear relationship between the number of years of smoking and the mean glycosylated hemoglobin (HbA1c). As the number of years of smoking rises there was an increase in the mean glycosylated hemoglobin levels (HbA1c).

## DISCUSSION

In the present study the two groups of subjects were of comparable age, Body Mass Index (BMI), Waist-to-hip ratio (WHR), physical activity and socio economic status. There is no significant increase in the fasting serum glucose levels between the smokers and non-smokers. The cigarette smokers have significant increase in the glycosylated hemoglobin levels when compared to the non-smokers.

This result is in agreement with the studies of Martin Urberg et al,<sup>[19]</sup> 2011 and EPIC-Norfolk study by Lincoln et al 2001.<sup>[11]</sup>

The link between cigarette smoking and the increased glycosylated hemoglobin may be due to the nicotine, which has been demonstrated to increase plasma levels of norepinephrine and epinephrine.<sup>[2]</sup> The increased catecholamines in the plasma have been known to cause increased hepatic glycolysis and gluconeogenesis.<sup>[1]</sup> The catecholamines might reduce the number of insulin binding sites as well as decrease the synthesis of glucose transporters.<sup>[20]</sup>

Smoking may directly impair insulin sensitivity which is one of the key determinant of glucose tolerance.<sup>[17]</sup> Smoking affects the mechanism

involving early steps in insulin action (eg. Signal transduction, glucose transport and/ or glucose phosphorylation) or by mechanisms operating simultaneously on different biochemical pathways.<sup>[7]</sup> The studies by Vani Gupta et al,<sup>[20]</sup> 2006 revealed that the smokers are prone for diabetes because of hyperinsulinemia and hyperglycemia and decreased insulin sensitivity.

An alternative explanation for an apparent effect of cigarette smoking and glucose tolerance would be through increased oxidative stress. This is known to be increased in cigarette smoking and the increased oxidative stress may impair insulin action.<sup>[12,13]</sup>

Further in the present study there is an increase in the level of mean glycosylated hemoglobin in smokers with increase in the number of years of smoking. The association of smoking with HbA1c suggests long term effects that may lead to increased risk of diabetes complications including cardiovascular disease.

## CONCLUSION

The results from the present study provide evidence of an increased glycosylated hemoglobin (Hb A1c) in non-diabetic smokers compared to the non-diabetic non-smokers. Smokers have been found to be at high risk for the development of diabetes mellitus. Hence this is a strong motivating factor for smokers to discontinue smoking early.

**Limitation:** The smokers differ widely in their smoking technique, making quantitation of the nicotine dose absorbed by an individual smoker and from an individual cigarette is difficult.

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