

The predominant role of smoking in clinical manifestation of type-II diabetes mellitus

Running Head: HbA1c in smokers and Non-smokers with Type-II Diabetes

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Abstract

Background: Type-II diabetes mellitus (T2DM) is a chronic disease characterised by persistent hyperglycemia and is associated with many complications and high morbidity. Smoking is a risk factor that can precipitate many complications of diabetes, including increases in HbA1c levels in patients with T2DM.

Materials and Methods: The study population included 100 type II diabetic male patients with a history of moderate smoking and 100 type II diabetic male patients with no smoking history. HbA1c levels were estimated using Microlab 300 at wavelength 415 nm against water as a blank (Fast Ion-Exchange Resin Separation Method).

Results and Conclusion: There was a significant increase after a period of 4 months in blood HbA1c levels ($p < 0.000$) in type 2 diabetics with a history of smoking. On the contrary, there was no significant increase ($p > 0.05$) in HbA1c levels in type 2 diabetes mellitus nonsmokers. A significant increase was observed in HbA1c in smokers as compared to non-smokers. They were concluding that smoking affects the HbA1c level but no other factors.

Key Words: Type-II diabetes mellitus, HbA1c, smokers, Non-smokers.

Introduction

Diabetes can occur when the pancreas does not secrete enough insulin or if the cells of the body become resistant to insulin; hence, the blood glucose cannot be transported into the cells, which then leads to serious complications. The classic symptoms of diabetes are frequent urination, excessive thirst and appetite, hyperglycemia, and generalised weakness. Because these symptoms are not very serious, many patients with diabetes do not seek medical care. In fact, more than 10 million Americans have diabetes, but fewer than half know that they have it or have ever consulted a physician¹.

Glycated haemoglobin (HbA1c) is a form of haemoglobin that is measured to identify the three-month average plasma glucose concentration. The limitation to a three-month average is because the lifespan of RBCs is three months². Ketoamine reactions between glucose and free amino groups on the alpha and beta chains of haemoglobin lead to the formation of glycated haemoglobin³. The HbA1c fraction of haemoglobin is highly elevated in diabetic patients with prolonged hyperglycemia. HbA1c levels below 5.7% indicate normal glucose tolerance, while levels between 5.7% and 6.4% indicate impaired glucose tolerance. A HbA1c value of 6.5% or more confirms diabetes mellitus. Obesity is one of the most important risk factors for type 2 diabetes⁴. Smoking has also been linked to type 2 diabetes, with heavy smokers being at a higher risk. The risk persists for approximately ten years after smoking cessation⁵. Cigarette smoking is

responsible for many systemic effects, including endothelial dysfunction, oxidative stress, and systemic inflammation. These factors are responsible for insulin resistance and type 2 diabetes mellitus. Smoking causes inflammation of the pancreas with damage to the cells of Langerhans. All these factors then lead to the development of diabetes mellitus⁶. The effect of quitting smoking has a remarkable effect on diabetes. The incidence of vascular complications is significantly reduced in non-smokers compared to smokers⁷.

Materials and methods

This was a descriptive, comparative research study. The study was conducted at the Medical Outpatient Department (OPD) of Khyber Teaching Hospital, Peshawar. The laboratories of the Pakistan Health Research Council (PHRC), Research Center Khyber Medical College, Peshawar, were utilised for HbA1c estimation. A total of 200 patients with type II diabetes mellitus were selected for this study and divided into two main groups:

Group 1: This group contained 100 male patients with type II diabetes mellitus who had a history of smoking.

Group 2: This group acted as a control and consisted of 100 nonsmoking male patients with type II diabetes mellitus.

Patients willing to cooperate and agree to participate in the study were selected. The written consent was taken from the patients on the prescribed form. The ethical approval was obtained according to guidelines laid down by the Office of Research, Innovation, and Commercialization (ORIC), Khyber Medical University (KMU). Patients fulfilling the selection criteria, i.e., male diabetics (Type 2) with a history of smoking or diabetes and an age of 30 years and above, were included. Patients with a history of type 1 diabetes mellitus and female patients, as the incidence of smoking is low in this region, were excluded, and patients with a history of liver or kidney disease were also not included.

Glycohemoglobin HbA1-Test (Fast Ion-Exchange Resin Separation Method) was used for the estimation of HbA1c. The test was performed by using Microlab 300 at 415 nm against water as a blank.

Statistical analysis

SPSS (version 24) and Microsoft Excel were used to analyse the data. The results obtained were entered into the computer for statistical analysis. The student t-test was applied for parametric numerical data, while the chi-square test was utilised for non-parametric categorical data. At the 95% CI, a P-value of 0.05 was considered statistically significant.

Results

A total of 200 copies of the questionnaire were distributed to type II diabetic patients, both smokers and nonsmokers; 190 copies were returned at a 95% rate. Thus, a total of 190 (n = 190) patients with type II diabetes mellitus were included in this research study. Out of the total patients, 95 (n = 95) were smokers and considered the study group. The second group also consisted of 95 (n = 95) type II diabetes mellitus patients with no smoking history, and this group is considered a control. The data were expressed as a standard deviation.

Socio-demographic Characteristics of Nonsmokers

The socio-demographic characteristics of patients with type II diabetes mellitus without a history of smoking are shown in table 2. The total number of patients in this group was 95, with an age range of 30 to 70 years. The patients with an age of 30–40 were 10 (10.53%), those with an age of 41–50 were 30 (31.58%), those with an age of 51–60 were 37 (38.94%), and those with an age of 61–70 were 18 (18.95%). Table 2 also shows the marital status of the patients. The majority of patients, 83 (87.37%), were married; the singles were 05 (05.26%); 03 (03.16%) were divorced; and 04 (4.21%) were widowed (Table 1).

| Variables | Responses | Frequency (N) | Percentage (%) |
|--------------------|-------------------------|---------------|----------------|
| Age of Patients | 30-40 | 12 | 12.63 |
| | 41-50 | 30 | 31.59 |
| | 51-60 | 35 | 36.84 |
| | 61-70 | 18 | 18.94 |
| | Total | 95 | 100 |
| Marital Status | Married | 84 | 88.44 |
| | Single | 07 | 7.36 |
| | Divorced | 01 | 1.05 |
| | Widowed | 03 | 3.15 |
| | Total | 95 | 100 |
| Educational Status | Primary Education | 52 | 54.73 |
| | Secondary Education | 30 | 31.57 |
| | Tertiary Education | 03 | 3.15 |
| | None | 10 | 10.55 |
| | Total | 95 | 100 |
| Occupation | Government Job | 23 | 24.23 |
| | Shopkeepers | 34 | 35.78 |
| | Working on daily wages | 20 | 21.05 |
| | Farmers | 18 | 18.94 |
| | Total | 95 | 100 |
| Smoking Status | Daily | 84 | 88.44 |
| | Thrice a week | 07 | 7.36 |
| | Twice a week | 02 | 2.10 |
| | Occasionally when tense | 02 | 2.10 |
| | Total | 95 | 100 |

Table 1: Socio-demographic characteristics of Smokers

Table 2 also shows the educational status of the patients. The majority of patients, i.e., 50 (52.63%), had primary education; the patients who received secondary education were 32 (33.68%); and six (6.33%) got tertiary education. The number of patients who did not go to school was 7 (7.36%). The occupational status of patients is also given in Table 2. The employees of provincial or local government were 25 (26.32%), shopkeepers were 32 (33.68%), those working on daily wages were 17 (17.89%), and farmers were 21 (22.11%).

Table 2 and Fig 1 show age-wise distribution and frequency of age group of patients of type-II diabetes mellitus in smoker and nonsmoker groups. The mean age group of smokers was

50.04±4.54, while the nonsmoker group was 49.16±4.42 years with no significant difference ($P < 0.194$).

| Variables | Responses | Frequency (N) | Percentage (%) |
|--------------------|-------------------------------|---------------|----------------|
| Age of Patients | 30-40 | 10 | 10.53 |
| | 41-50 | 30 | 31.58 |
| | 51-60 | 37 | 38.94 |
| | 61-70 | 18 | 18.95 |
| | Total | 95 | 100 |
| Marital Status | Married | 83 | 87.37 |
| | Single | 05 | 05.26 |
| | Divorced | 03 | 03.16 |
| | Widowed | 04 | 04.21 |
| | Total | 95 | 100 |
| Educational Status | Primary Education | 50 | 52.63 |
| | Secondary Education | 32 | 33.68 |
| | Tertiary Education | 06 | 6.33 |
| | None | 07 | 7.36 |
| | Total | 95 | 100 |
| Occupation | Government Job | 25 | 26.32 |
| | Shop keepers, Carpenters etc. | 32 | 33.68 |
| | Working on daily wages | 17 | 17.89 |
| | Farmers | 21 | 22.11 |
| | Total | 95 | 100 |

Table 2: Socio-demographic characteristics of Non Smokers

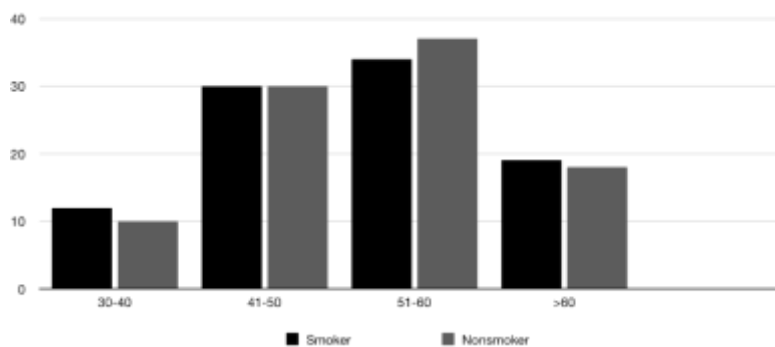


Fig 1: Age-wise Distribution in Smokers and Non Smokers

In the present study, different age groups were selected from both smokers and nonsmokers with type II diabetes mellitus. The smoker and nonsmoker groups were subdivided into four subgroups. Table 3 shows that the first subgroup is 30-40 years old, the second is 41-50 years old, the third is 51-60 years old, and the fourth is 61-70 years old.

| Age group | Smoker | Non-Smoker |
|-----------|-----------|------------|
| 30-40 | 12 (12.6) | 10 (10.5) |
| 41-50 | 30 (31.6) | 30 (31.6) |
| 51-60 | 34 (35.8) | 37 (38.9) |
| > 60 | 19 (20.0) | 18 (18.9) |
| Total | 95 (100) | 95 (100) |

Table 3: Age wise distribution of various groups under study

Table 4 also shows blood HbA1c levels in the nonsmoker group of diabetes mellitus. In the first sub-age group (30-40 years), the initial HbA1c levels were $6.80 \pm .25$, while after four months, the levels were $6.88 \pm .29$, which is not significant (p-value .545). The initial blood HbA1c levels in the second sub-age group (41-50 years) were $7.15 \pm .30$, while after four months, the levels were $7.35 \pm .27$. The result is significant (p-value .011). The initial blood HbA1c levels in the third sub-age group (51-60 years) were $7.29 \pm .35$, while after four months, the levels were $7.38 \pm .31$. The difference is not significant (p-value .278). The initial blood HbA1c levels in the fourth sub-age group (61-70 years) were $7.48 \pm .37$, while after four months, the levels were $7.55 \pm .26$. Again, the difference is not significant (p-value .495).

| Age Group | Smoker (Mean \pm SD) | | p.value | Non-Smoker (Mean \pm SD) | | p.value |
|-----------|------------------------|----------------|---------|----------------------------|----------------|---------|
| | Initial | After 4 months | | Initial | After 4 months | |
| 30-40 | 7.77 \pm .44 | 8.18 \pm .46 | .043 | 6.80 \pm .25 | 6.88 \pm .29 | .545 |
| 41-50 | 7.72 \pm .31 | 8.42 \pm .40 | .000 | 7.15 \pm .30 | 7.35 \pm .27 | .011 |
| 51-60 | 7.71 \pm .41 | 8.72 \pm .40 | .000 | 7.29 \pm .35 | 7.38 \pm .31 | .278 |
| > 60 | 7.85 \pm .38 | 8.94 \pm .48 | .000 | 7.48 \pm .37 | 7.55 \pm .26 | .495 |

Table 4: Comparison of HbA1c levels in different age groups under study

Fig. 2 presents the frequency distribution of HbA1c levels in patients with type II diabetes mellitus with a history of smoking and those without a history of smoking at the start of this research study. Fig. 3 shows the frequency distribution of HbA1c levels in patients with type II diabetes mellitus with a history of smoking and those without a history of smoking after four months.

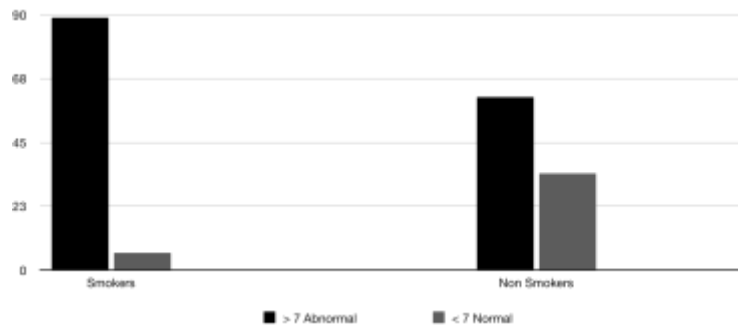


Fig 2: Frequency Distribution of HbA1c in both Smokers and Nonsmokers (Initial)

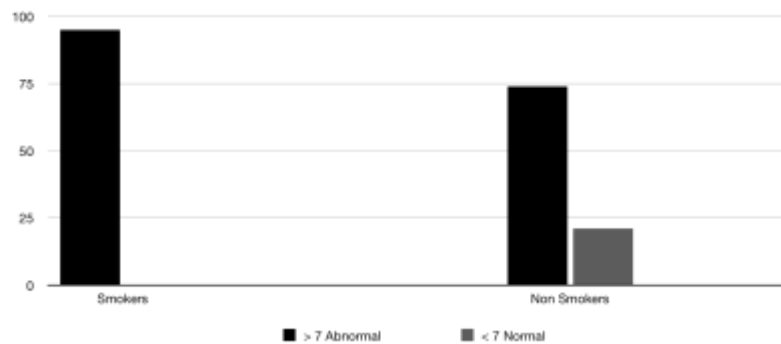


Fig 3: Frequency Distribution of HbA1c in both Smokers and Nonsmokers (After 4 months)

Discussion

Diabetes mellitus has been chosen for this research work as this disease is a significant public health problem and is associated with many complications over time. The common complications seen are ischemic heart disease, peripheral vascular disease, hypertension causing stroke, blindness due to retinopathy, and kidney failure due to nephropathy⁸. Similarly, if a person has type II diabetes and smokes, their risk factors increase⁹.

The increased mortality rate in patients with type-II diabetes mellitus is mainly due to complications associated with this disease¹⁰. Family history of diabetes, hypertension, increased body weight, elevated blood lipid levels, and smoking are all risk factors for type II diabetes mellitus¹¹. This study indicates a significant increase in blood HbA1c levels in patients with type II diabetes mellitus who smoke. This data contradicts McCulloch P et al.¹² findings. They worked on a research project in 2002 and claimed that smoking did not significantly affect HbA1c levels in patients with type II diabetes mellitus. The results of this study, however, are according to the findings of Nilsson¹³. They worked on a research project in Sweden in 2004 and discovered that smokers with type 1 and type II diabetes had higher mean HbA1c levels than nonsmokers. Passive smoking is equally hazardous to people's health and can produce all the adverse effects caused by active smoking. Most diabetics smoke cigarettes to control their body weight. They also smoke to relieve anxiety and tension and feel more confident and energetic¹⁴.

Conclusion

There was a significant increase in blood HbA1c levels in patients with T2DM and a history of smoking. Some researchers are of the view that there is a significant correlation between blood HbA1c levels and retinopathy and nephropathy in patients with diabetes mellitus¹⁵. Government and non-governmental organisations should take an active role regarding awareness and cessation of smoking in the general public and among patients with type II diabetes mellitus.

References

1. Adewole SO and Ojewole JAO: Protective effect of *Annona muricata* Linn. (Annonaceae) leaf aqueous extract on serum lipid profile and oxidative stress in hepatocytes of streptozotocin-treated diabetic rats. *Afr J Trad Cam* 2009; 6(1): 30-41.
2. Kumar PJ & Clark MI (2012): Diabetes mellitus and other disorders of Metabolism, Chapter 20 in Text book of Clinical Medicine, 8th Edition, Saunders Elsevier, 1001-10045.
3. American Diabetes Association. Standards of medical care in diabetes—2014. *Diabetes Care* 2014;37:S14-S80.
4. Jensen MD. Obesity. In: Goldman L, Schafer AI, eds. *Goldman's Cecil Medicine*. 25th ed. Philadelphia, PA: Elsevier Saunders; 2016: chap 220.

5. Luo J, Rossouw J, Tong E, Giovino GA, Lee CC, Chen C, et al. Smoking and diabetes: does the increased risk ever go away? *American Journal of Epidemiology*. 2013; 178 :(6)937–945.
6. Wannamethee SG, Shaper AG, Perry IJ. Smoking as a modifiable risk factor for type 2 diabetes in middle-aged men. *Diabetes Care* 2001; 24:1590-5.
7. Buysschaert M, Ddramalx A S, Wallemacq P, Hermans M.: Hyperhomocysteinemia in type 2 diabetes: Relationship to macro angiopathy, nephropathy and insulin resistance. *Diabetes care* 2000; 23: 1816-1822.
8. Bays HE, Chapman RH and Grandy S: The relationship of body mass index to diabetes mellitus, hypertension and dyslipidemia: comparison of data from two national surveys. *Int J Clin Pract* (2007), May 1, 61(5):737-747.89
9. Greenland S: Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. *American Journal of Epidemiology* 2004; 160(4):301-305.
10. Richard PS, Robert MS and Stanton AG: Reduced incidence of admissions for myocardial infarction associated with public smoking ban: before and after study: *British Medical Journal* (2004): 328:977.
11. Bays HE, Chapman RH and Grandy S: The relationship of body mass index to diabetes mellitus, hypertension and dyslipidemia: comparison of data from two national surveys. *Int J Clin Pract* (2007), May 1, 61(5):737-747.89
12. McCulloch P, Lee S, Higgins R, McCall K & Schade DS: Effect of smoking on hemoglobin A1c and body mass index in patients with type 2 diabetes mellitus: *Journal of Investigative Medicine* (2002) Jul; 50(4):284-7
13. Nilsson PM, Gudbjornsdottir S and Eliasson B: Smoking is associated with increased HbA1c values and micro albuminuria in patients with diabetes: *Diabetes Metab* (2004): Jun; 30(3): 261-8.

14. Jiang F, Chen M, Hu C. et al. Effects of active and passive smoking on chronic kidney disease in patients with type 2 diabetes mellitus. *Zhonghua Nei Ke Za Zhi* 2014. 53(11): 858-864.
15. Tapp RJ, Zimmet P and McCarty DJ: Diagnostic thresholds for diabetes; the association of retinopathy and albuminuria with glycaemia: *Diabetes Res Clin Pract* (2006): 73 (3), 315-21.