RESEARCH ARTICLE

Association between smoking and glycated hemoglobin in type II diabetes mellitus male patients visiting outpatient department: A hospital-based study

Shah Mohammad Abbas Waseem¹, Hamid Ashraf², Syed Haider Mehdi Husaini³, Syed Hilal Hussain⁴

¹Department of Physiology, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, ²Rajiv Gandhi Center for Diabetes and Endocrinology, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, ³Department of Medicine, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, ⁴MBBS Student, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Correspondence to: Shah Mohammad Abbas Waseem, E-mail: abbas14waseem5@gmail.com

Received: October 16, 2023; Accepted: November 23, 2023

ABSTRACT

Background: Smoking is emerging as a public health concern in India, with 30% of the population (majority males) consuming tobacco products. The risk of metabolic syndrome is 1.07–1.66 times higher in smokers. Both smoking and diabetes are expected to rise in India. Aims and Objectives: The association of smoking with glycated hemoglobin (HBA1C) was analyzed in the present study. The effect of tobacco on total leucocyte count (TLC) and HBA1C was also studied. Materials and Methods: The study included 150 male diabetics grouped into smoker and non-smoker categories. Currents were further categorized as per smoking intensity. TLC and HBA1C were evaluated, and the data were analyzed using appropriate statistical tests in SPSS 21.0 and Microsoft Excel. A P < 0.05 was taken as significant. Results: HBA1C increased significantly (P < 0.0101) with an increase in intensity of smoking, but the difference was insignificant between non-smokers and mild (P = 0.125) to moderate (P = 0.07) intensity smokers. TLC increased significantly with an increase in smoking intensity compared to non-smokers (P < 0.001). Differences in TLC were insignificant between mild smokers and non-smokers (P = 0.114). HBA1C and TLC were significantly (P < 0.001) raised in current smokers as compared to ex-smokers and non-smokers, but the difference between HBA1C in non-smokers and ex-smokers was insignificant (P = 0.534). TLC increased insignificantly in ex-smokers as compared to non-smokers (P = 0.129). Regression analysis showed that HBA1C was significantly higher in ex-smokers (β = 0.0438, P = 0.021) and current smokers (β = 0.682, P = 0.001) than non-smokers. With the increase in the severity of smoking, HBA1C was higher than in non-smokers, but the association was insignificant. A non-significant positive association was found between TLC and HBA1C in current smokers (r = 0.049, P = 0.781) and ex-smokers (r = 0.036, P = 0.824), and a non-significant (P = 0.745) negative association (r = -0.070) was found between two non-smokers. Conclusion: In smokers, HBA1C and TLC are higher and are further raised with increased smoking intensity.

KEY WORDS: Nicotine; Smoking; Non-Enzymatic Glycation; Gender; Blood Cells; Diabetes; Association; Correlation

INTRODUCTION

60–70 million Indians had diabetes in 2016, with reportedly a 3% mortality rate. Hyperglycemia-induced changes affect the body’s physiological systems.¹⁻² By 2030, it is expected that 522 million Indians will have diabetes, with the majority in the age group of 60–79 years.³ Tobacco is expected to kill
1.5 million people in 2020; by 2030, this figure will exceed 8 million. Smoking is emerging as a public health concern in India, with 30% of the population (majority males) consuming tobacco products.[4-7] The results of the study have shown poor glycemic control and higher glycated hemoglobin (HBA1C) levels in male diabetics who are smokers.[9] Furthermore, the risk of metabolic syndrome is 1.07–1.66 times higher in smokers. Smoking increases insulin resistance by causing lipolysis and the release of counter-regulatory hormones such as cortisol, growth hormone, adrenocorticotropic hormone, and catecholamines, and also affects the release of neurotransmitters such as gamma-aminobutyric acid, serotonin, and dopamine.[9,10] Tobacco and its constituent nicotine cause leukocytosis by increasing arachidonic acid metabolites, lymphocytic proliferation, and differentiation.[11] Leukocytosis in people with diabetes occurs due to increased advanced glycation end products, oxidative stress, inflammation, and angiotensin II, which indicates future macro- and micro-vascular complications, the extent of sugar control, and insulin resistance.[12] Positive associations between white blood count (WBC) and metabolic syndrome have been reported—smoking and its severity result in systemic inflammation and leukocytosis.[13] The risk of type 2 diabetes is higher with lymphocytosis and neutrophilia. Monitoring of WBCs as markers of inflammation can be used in each stage of diabetes for complications and disease progression. The likelihood of obesity, sedentary lifestyle, alcohol consumption, and smoking is associated with a higher quintile of leukocyte counts, as per an earlier report. Literature is suggestive of endothelial dysfunction in metabolic syndrome, which enhances leukocyte differentiation, thereby causing an increase in leukocyte counts.[14,15]

However, there are inconsistent reports on the association between total leukocyte count (TLC) and diabetes risk,[16,17] which requires further exploration. The relative risk of diabetes increases with the extent, duration, and severity of smoking due to an increase in C reactive protein or interleukin-6, an increase in insulin requirements either due to resistance or decrease in sensitivity, and also due to nicotine-induced apoptosis of beta cells of the pancreas.[18,19] Diabetes and smoking are expected to increase in the coming decade. Smoking, leukocytosis, and diabetes appear to be interlinked, but inconsistent reports and a paucity of data exist. Thus, the present study aimed to find the association between smoking, TLC, and HBA1C in male patients with diabetes and also study the effect of smoking intensity on study variables. The results and findings will add to the literature and enhance the data available on the subject of the study.

Aim and Objectives of the Study

The study was designed to find the association between smoking and HBA1C. The effects of smoking and its intensity (assessed by pack years) on HBA1C and TLC were also analyzed.

MATERIALS AND METHODS

The present study was a hospital-based cross-sectional study conducted in the Department of Physiology between August and October 2022. 150 type 2 diabetes mellitus patients (males between 30 and 60 years) attending the outpatient departments (OPDs) were included in the study. People with diabetes were selected based on the American Diabetes Association Classification.[20] They were divided into current smokers (n = 56), ex-smokers (n = 51), and non-smokers (n = 43) groups. Current smokers were further divided into mild (n = 15), moderate (n = 19), and severe (n = 22) intensity smoking categories based on pack years.[6-21] The study was a part of the research project approved by the Institutional Ethics Committee (Ref. Number IEC/662). Informed and written consent was obtained from the participants in the study.

Exclusion Criteria

Subjects unwilling to participate, patients with chronic kidney or liver disease, those receiving medications that resulted in hypoglycemia, <30, and more than 60 years of age were excluded from the study. Data on the dropouts were also not analyzed.

Blood collected in the EDTA vial was used to estimate HBA1C per the elsewhere method.[22] TLC was measured with the help of an automated analyzer (Beckman coulter) in the central lab.

Statistical Analysis

The data were presented as mean ± SD and analyzed using the R software using analysis of variance, Pearson’s correlation, and regression analysis. For regression analysis, HBA1C was taken as a dependent variable, and pack year smoking categories, i.e., no-smokers, current, and ex-smokers, were taken as independent variables. A P < 0.05 was taken as statistically significant.

RESULTS

A significant difference (P = 0.038) was found in the mean age of current smokers (43.62 ± 7.25), ex-smokers (46.85 ± 8.01), and non-smokers (39.87 ± 7.88). The HBA1C levels were significantly (P < 0.001) higher in current smokers (7.66 ± 0.46) as compared to ex-smokers (7.34 ± 0.35) and non-smokers (7.28 ± 0.26), but the difference was non-significant (P = 0.534) between non-smokers and ex-smokers. Similarly, a significant difference (P < 0.001) was observed in TLC between current smokers (8130.97 ± 1175.28), ex-smokers (7173.73 ± 1426.89), and non-smokers (6671.50 ± 1131.91). TLC was higher in ex-smokers than non-smokers, but the difference was insignificant (P = 0.129) [Table 1]. Current smokers were...
divided into three categories, i.e., mild (12.71 ± 0.92), moderate (16.19 ± 1.60), and severe (21.44 ± 0.93) based on pack years. A significant difference (P < 0.001) in pack years was found between current smokers [Table 2]. HBA1C (%) in non-smokers was 7.28 ± 0.26, and it increased further with an increase in smoking intensity, and differences were statistically significant (P < 0.001). The difference (HBA1C) was non-significant between non-smokers and mild (P = 0.125) to moderate (P = 0.007) intensity smokers. TLC increased significantly with an increase in smoking intensity compared to non-smokers (P < 0.001). A non-significant difference in TLC was found between non-smokers and mild-intensity smokers (P = 0.114) [Table 3]. Compared to non-smokers, HBA1C levels were significantly higher in ex-smokers (β = 0.0438, P = 0.021) and current smokers (β = 0.682, P = 0.001). With the increase in the severity of smoking, HBA1C levels increased compared to non-smokers, but the association was insignificant [Table 4]. A non-significant positive association between TLC and HBA1C in the current (r = 0.049, P = 0.781) and ex-smokers (r = 0.036, p = 0.824) was found. However, a non-significant (P = 0.745) negative association (r = -0.070) was found between two variables in non-smokers [Table 5].

**DISCUSSION**

The results of our study showed significantly higher HBA1C and TLC in current smokers as compared to ex-smokers and non-smokers. With the increase in intensity of smoking (as assessed by pack years), HBA1C and TLC were raised significantly. TLC and HBA1C showed a non-significant positive association in current and ex-smokers, and the association was negative between the two variables in non-smokers. With an increase in smoking intensity, HBA1C increased, but the association was non-significant.

Reportedly, there are issues with fasting blood glucose as a reliable indicator of diabetes due to non-disclosure or hesitancy in reporting meals or types of food ingested before the sugar testing. HBA1C values are a reliable test for sugar control testing. Microvascular complications are reportedly lower in people with diabetes with lower values of HBA1C.[24]

In the present study, TLC was significantly higher in smokers than non-smokers, and it was higher in current smokers and increased with an increase in the intensity of smoking. Studies have reported that TLC in people with diabetes with a history of tobacco is higher,[25] which could be attributed to a nicotine-induced increase in white blood cells. Furthermore, smoke acts as an irritant, thereby triggering an immune response and resulting in the recruitment of cells for acute and chronic inflammation. An increase in WBC count results in microvascular complications,[26-28] which require attention in people with diabetes and a history of smoking. The mean values of TLC in our study were higher in ex-smokers than non-smokers, which could be explained based on earlier studies, which have shown that an increase in TLC depends

**Table 1: Difference in age and HBA1C and TLC on the basis of smoking status of study subjects**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Current (n=56)</th>
<th>Ex-smoker (n=51)</th>
<th>Non-smoker (n=43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.62±7.25</td>
<td>46.85±8.01</td>
<td>39.87±7.88</td>
<td>0.038</td>
</tr>
<tr>
<td>HBA1C (%)</td>
<td>7.66±0.46</td>
<td>7.34±0.35</td>
<td>7.28±0.26</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TLC (cell/mm$^3$)</td>
<td>8130.97±1175.28</td>
<td>7173.73±1426.89</td>
<td>6671.50±1131.91</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*P value is significant at P<0.001. **Difference between non-smoker and ex-smoker was non-significant (P=0.534). *Non-significant difference was found between non-smoker and ex-smoker (P=0.129). HBA1C: Glycated hemoglobin, TLC: Total leukocyte count

**Table 2: Comparison of pack years in current smokers**

<table>
<thead>
<tr>
<th>Category</th>
<th>Mild (n=15) (10–14 pack years)</th>
<th>Moderate (n=19) (15–19 pack years)</th>
<th>Severe (n=22) (&gt;20 pack years)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smokers</td>
<td>12.71±0.92</td>
<td>16.19±1.60</td>
<td>21.44±0.93</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 3: Comparison on the basis of severity of smoking as per pack years**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild (n=15) (10–14 pack years)</th>
<th>Moderate (n=19) (15–19 pack years)</th>
<th>Heavy (n=22) (&gt;20 pack years)</th>
<th>Non-smoker (n=43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBA1C (%)</td>
<td>7.49±0.35</td>
<td>7.51±0.43</td>
<td>8.00±0.43</td>
<td>7.28±0.26</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>P=0.125 and 0.07 respectively*</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TLC (cell/mm$^3$)</td>
<td>7653.72±1229.97</td>
<td>8228.15±947.85</td>
<td>8493.36±1303</td>
<td>6671.50±1131.91</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>P=0.125 and 0.07 respectively*</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>7.28±0.26</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*No significant difference between non-smoker as compared to mild and moderate intensity smokers (P=0.125 and 0.07, respectively). **No significant difference between non-smoker and mild-intensity smokers (P=0.125). HBA1C: Glycated hemoglobin, TLC: Total leukocyte count
The results of our study highlighted a significant association between current smoking category and severity of smoking, i.e., current smokers with greater pack years had higher values of HBA1C than never-smokers, even if the duration of quitting smoking is equal to or more than a decade in the former.

Contradictory results indicating that ex-smokers may not be at high risk of developing diabetes have also been reported.\cite{38} Smoke contains 500–3500 compounds in both gaseous and particulate forms, which affect glucose homeostasis\cite{39} and thus require extensive research, provided the effects may be widespread and may remain for a more extended time. Quitting smoking acts like a two-way sword as far as sugar control is concerned. There are contradictory reports on the effects of quitting smoking and glycemia control. Some studies have suggested improvements in sugar control, but at the same time, literature also suggests that cessation leads to weight gain, resulting in poor glycemic control. Smoking increases the deposition of metabolically active adipose tissue, resulting in poor diabetes control and acting as a risk for diabetes.\cite{40,41} The results of our study highlighted that HBA1C values were higher in middle-aged smokers and even ex-smokers. Thus, extensive follow-up studies, including counseling and motivation of patients with diabetes to stop smoking and monitoring strategies for successful implementation of smoking cessation, will yield better results.

The importance of our study lies in the fact that smoking is a modifiable risk factor for diabetes. Smoking-induced derangement in glucose control is associated with micro- and macro-vasculature complications. Approximately 19% of cases of diabetes are directly linked to smoking,\cite{42} and thus, smoking habits need to be thoroughly evaluated in people with diabetes in OPD at the time of diagnosis, which is expected to reduce not only the complications but also improve the prognosis and aid in treatment. WBC counts in diabetes can also be used as markers of inflammation, disease progression, and complications.

**Limitations and Improvements**

Smoking appears to be a modifiable risk factor for diabetes. Socioeconomic conditions and the environment influence smoking habits and may co-exist with alcohol consumption.

---

**Table 4: Association of smoking category and severity with HBA1C in study subjects**

<table>
<thead>
<tr>
<th>Smoking category and severity</th>
<th>HBA1C</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smoker</td>
<td></td>
<td>Reference</td>
</tr>
<tr>
<td>Current</td>
<td>0.0682</td>
<td>0.0211</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.0438</td>
<td>0.0199</td>
</tr>
</tbody>
</table>

**Table 5: Correlation of TLC with HbA1c in diabetics as per the smoking category**

<table>
<thead>
<tr>
<th>Smoking category</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smokers (n=56)</td>
<td>0.049</td>
<td>0.781</td>
</tr>
<tr>
<td>Ex-smokers (n=51)</td>
<td>0.036</td>
<td>0.824</td>
</tr>
<tr>
<td>Non-smokers (n=43)</td>
<td>−0.070</td>
<td>0.745</td>
</tr>
</tbody>
</table>

HBA1C: Glycated hemoglobin, TLC: Total leucocyte count

upon the intensity of smoking and duration of quitting. Studies have shown that if the duration of quitting is more than a decade, then the rise of TLC is less compared to those for whom the duration is less than a year.\cite{29}

In our study, mean values of HBA1C were higher in current smokers than in ex-smokers and non-smokers. Results align with earlier studies, which have reported that the risk of diabetes in current smokers is higher.\cite{36} Results of the study done by Hong et al. found that the mean values of HBA1C were higher in current heavy smokers than current light smokers past and never smokers, indicating a relationship between HBA1C and smoking.\cite{31}

In our study, HBA1C was raised with an increase in the severity of smoking, i.e., current smokers with greater pack years had higher values of HBA1C. Results of the study done by Braffett et al. (2019) demonstrated that the values of HBA1C were more elevated in current smokers as compared to never smokers or ex-smokers, and the increase in HBA1C greater in patients with a history of more than ten pack years.\cite{32} Higher HBA1C indicates poor glycemic control and is thus expected to worsen the complications associated with diabetes in the future.\cite{33-35}

Our study found a significant association between current smokers and HBA1C compared to never-smokers, which increased with the severity of smoking. Studies have reported a higher risk of diabetes in smokers than non-smokers and that the risk increases with increased smoking intensity. The relation could be attributed to smoking-induced inflammation, an increase in metabolic active adipose tissue, thus resulting in insulin activity impairment or even resistance, poor glycemic control, and smoking-induced oxidant anti-oxidant imbalance.\cite{36} Similarly, studies have reported that the risk of diabetes in smokers depends on the severity of smoking. Reportedly, the ex-smokers had <25% risk of diabetes. The risk of diabetes is reported to be 60% in those who smoke more than 20 cigarettes/day, and the risk reduces to 30% if the amount is reduced.\cite{19} A previous study reported a smoking history in patients with diabetes.\cite{37} A significant association was found between HBA1C and ex-smokers in our present study. Studies have reported that the duration of quitting smoking influences the risk of developing diabetes. Reportedly, the risk of diabetes is 20% higher in male smokers than never-smokers, even if the duration of quitting smoking is equal to or more than a decade in the former.
and the intake of other substances of abuse, which require inclusion and investigation. Both effects, as well as the duration of cessation and quitting smoking, require evaluation. Comparative studies between diabetic and non-diabetic subjects with and without smoking histories and subsequent follow-up would improve the results. An association between smoking and its intensity and duration has also been found in smokers without diabetes, thus predisposing them to the risks of diabetes in the future and associated complications. Therefore, a large-scale study on the effects of smoking on glucose homeostasis is required.

CONCLUSION

Smoking is associated with an increase in TLC and HBA1C. In the present study, people with diabetes and a smoking history had higher HBA1C and white blood cell counts. Current smokers with a higher severity of smoking had higher HBA1C and TLC, indicating the role of smoking in diabetes. Both smoking and diabetes are expected to rise in the coming decade in India, and since there appears to be a link between the two, smoking history must be thoroughly investigated in diabetics to reduce future complications and aid in better management.

REFERENCES


How to cite this article: Waseem SM, Ashraf H, Husaini SH, Hussain SH. Association between smoking and glycated hemoglobin in type II diabetes mellitus male patients visiting outpatient department: A hospital-based study. Natl J Physiol Pharm Pharmacol 2024;14(Online First). DOI: 10.5455/njppp.2023.13.10492202323112023

Source of Support: Nil, Conflict of Interest: None declared.