Smoking habits and the risk of type 2 diabetes: A case-control study
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Abstract

Aim. – The objective of the study was to assess the relationship between smoking and the risk of type 2 diabetes.

Subject and methods. – This case-control study included 234 cases with newly confirmed diagnoses of type 2 diabetes and 468 controls who were free of the disease in 2001. Cases and controls were matched by gender and age (±5 years). A questionnaire was used to collect information on the possible risk factors of type 2 diabetes. Clinical measurements were taken in accordance with the recommendations of the WHO. Fasting plasma glucose and triglycerides were also measured, and the glucose tolerance test was performed in the controls. The odds ratios (OR) and 95% confidence intervals (CI) for type 2 diabetes were calculated using conditional logistic regression.

Results. – The diabetes cases had significantly less education, more first-degree relatives with a positive family history of diabetes and higher body mass index (BMI) scores compared with the controls. Also, after adjusting for possible confounders, an increased risk of type 2 diabetes was determined for current smokers (OR = 2.41; 95% CI 1.07–5.44) vs. non-smokers. In addition, there was an association between the disease and duration of smoking (OR = 2.47; 95% CI 1.03–5.93 for 40 years or more) vs. non-smokers, and those who had been smokers for 10 or more pack-years had twice the risk of diabetes (OR = 2.17; 95% CI 1.07–4.40) vs. non-smokers. There were no significant associations found between the risk of type 2 diabetes and number of cigarettes smoked per day or stopping smoking.

Conclusion. – Our data confirms that smoking may be an independent risk factor for type 2 diabetes.

Keywords: Smoking; Type 2 diabetes; Case-control study; Risk factors for diabetes

Résumé

Tabagisme et risque de diabète de type 2 : étude cas–témoins.

Le but de l’étude était d’évaluer les liens éventuels entre tabagisme et risque de diabète de type 2 (DT2).

Sujets et méthodes. – Deux cent trente-quatre DT2 de découverte récente et 468 témoins non-diabétiques ont été inclus dans une étude cas–témoins menée en 2001. Les diabétiques et les témoins ont été appariés pour l’âge (±5 ans) et le sexe. Un questionnaire a été utilisé pour le recueil des données sur les facteurs de risque possibles de DT2. Les mesures anthropométriques ont été réalisées selon les recommandations de l’OMS. Glycémie à jeun et les triglycérides ont été mesurés pour tous les sujets. L’épreuve de tolérance au glucose a été effectuée pour les témoins. Les odds ratios (OR) et les intervalles de confiance à 95 % (IC) de développement d’un DT2 ont été calculés avec un modèle de régression logistique conditionnelle.

Résultats. – Les DT2 comparés aux témoins avaient un niveau d’éducation significativement inférieur, des antécédents familiaux de DT2 plus fréquents et un indice de masse corporelle plus élevé. Après ajustement pour les facteurs confondants possibles, le risque de DT2 était plus élevé chez les fumeurs actuels (OR = 2.41 ; IC 1.07–5.44 vs. non-fumeurs). En outre, il existait une association entre le DT2 et la durée du tabagisme (OR = 2.47; IC 1.03–5.93 pour une durée de plus de 40 ans vs. non-fumeurs). Les sujets qui avaient fumé dix paquets par an ou plus avaient un risque de développer un DT2 deux fois plus élevé (OR = 2.17 ; IC 1.07–4.40 vs. non-fumeurs). Il n’y avait pas d’association significative entre le risque de DT2 et le nombre de cigarettes fumées par jour ni l’arrêt de tabagisme.

Conclusion. – Ces données confirment que le tabagisme peut être un facteur de risque indépendant de développer un DT2.

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Mots clés : Tabagisme ; Diabète sucré de type 2 ; Étude cas–témoins ; Facteurs de risque de diabète de type 2
1. Introduction

Diabetes mellitus, one of the main public health issues today, is becoming a worldwide pandemic. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 [1]. In Lithuania, type 2 diabetes has become more prevalent and is now an important health issue. The prevalence of the disease is 4.5% among adults aged 35–65 years in Kaunas [2], and the numbers of those with diabetes are increasing along with population growth, age, urbanization, and the growing prevalence of obesity and physical inactivity [3].

Smoking exacts indisputable and devastating damage on public health. Tobacco use is the most important cause of preventable morbidity and mortality around the world [3], and is responsible for one in 10 deaths among adults worldwide. In 2005, tobacco caused 5.4 million deaths, or an average of one death every six seconds. The death toll is projected to reach 8.3 million by 2030 if the current trends continue [4]. On average, 29% of people around the world are smokers. Smoking is more common among men (47.5% of smokers are male) than among women (10.3%) [4]. In Lithuania, the prevalence of smoking was 12.8% among women and 43.7% among men in 2002 [5]. According to data from Haire-Joshu et al. [6], the prevalence of smoking in patients with diabetes is similar to that found in the general population.

However, there have been no epidemiological studies of type 2 diabetes carried out in Lithuania. For this reason, we conducted an outpatients-based case-control study in Kaunas. Our objective was to assess the relationship between smoking and the risk of type 2 diabetes.

2. Materials and methods

Our case-control study included 234 patients, aged 35–86 years old, with newly confirmed diagnoses of type 2 diabetes. These cases were all diagnosed according to criteria recommended by the World Health Organization (WHO) between 1 January 2001 and 31 December 2001. Controls were recruited from patients attending the same clinic. Altogether, we included 468 controls who did not have impaired fasting glucose or type 2 diabetes following a glucose tolerance test. These controls were individually matched to the patients by gender and age (±5 years). There were two controls for each of our studied cases.

Information concerning age, gender, family history of diabetes, level of education, occupational and marital status, eating habits, alcohol consumption, cigarette smoking, physical activity and stress levels was collected by questionnaire. All study subjects were asked to fill out the questionnaire by themselves.

Clinical measurements were taken according to the WHO guidelines [8]. Height and weight were measured in duplicate. Height was measured without shoes in centimetres (0.1 cm accuracy). Weight was measured with each subject wearing light clothing in kilograms (0.5 kg accuracy). Body mass index (BMI) was calculated as weight (kg)/height (metres) squared [9]. Waist circumference was measured by holding the non-stretchable measuring tape snugly around the waist, defined as the midpoint between the bottom rib and tip of the hipbones, and hip circumference was measured at the level of the femoral trochanter in centimetres (0.1 cm accuracy).

Laboratory blood tests included fasting blood samples drawn from the elbow vein, with venous plasma samples analyzed for glucose and triglycerides (TG). Venous plasma glucose was estimated by the GOD–PAP method (Epinendorf analyzer, Germany). According to the 1999 WHO recommendations, oral glucose tolerance tests for assessing carbohydrate disorders were performed and evaluated in the study subjects. TG were estimated by the GPO–PAP method (Randox analyzer, UK).

Smoking was assessed according to:

- smoking habits: non-smoker, ex-smoker, infrequent smoker, current smoker;
- duration of smoking: non-smoker, less than 19 years, 20–39 years, over 40 years;
- number of cigarettes smoked per day: non-smoker, 1–9 cigarettes per day, more than 10 cigarettes per day;
- pack-years (number of cigarettes smoked per day/20 multiplied by smoking time [years]);
- non-smoker, less than 9 years, more than 10 years [10];
- smoking cessation: non-smoker, less than 19 years, more than 20 years.

No data for smoking pipes or cigars were collected from the subjects.

BMI was grouped according to those who were: 18.5–24.9 kg/m², 25–29.9 kg/m² and more than 30 kg/m². Waist circumference was grouped as those who were:

- less than 80 cm for women and less than 94 cm for men;
- 80–88 cm for women and 94–102 cm for men;
- greater than 88 cm for women and greater than 102 cm for men.

A family history of diabetes was divided into two categories: first-degree relatives with a family history of diabetes and first-degree relatives without a family history of diabetes. Level of education (number of years) was divided into three categories: less than 10 years, 11–13 years and greater than 14 years. Marital status was assessed by four groups: married/living together, divorced/separated, single and widow/widower. Plasma TG was grouped into those with less than 1.7 (mmol/L) and those with over 1.7 (mmol/L).

Conditional logistic regression was used to calculate the odds ratios (OR) and corresponding 95% confidence intervals (CI) for diabetes in relation to exposures of interest. Variables (such as a family history of diabetes, BMI, waist circumference, plasma TG and education level) were retained in models as confounders when their inclusion changed the value of the OR by more than 10% in any exposure category.

All reported test trend significance levels (p values) were two-sided [11]. The χ² test was used to calculate the difference between proportions. The level of significance was set at 5%. All calculations were performed using the STATA 7 software programme.
Table 1
Demographic characteristics of the study cases and controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Cases</th>
<th>Controls</th>
<th>( p ) value for ( \chi^2 )</th>
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<tr>
<td></td>
<td></td>
<td>( n )</td>
<td>%</td>
<td>( n )</td>
</tr>
<tr>
<td>Gender</td>
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<td>28.21</td>
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<tr>
<td></td>
<td>Female</td>
<td>168</td>
<td>71.79</td>
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<tr>
<td>Age (years)</td>
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<td>5.13</td>
<td>22</td>
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<tr>
<td></td>
<td>45–54</td>
<td>21</td>
<td>8.97</td>
<td>44</td>
</tr>
<tr>
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<td>55–64</td>
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<td>( \geq 65 )</td>
<td>111</td>
<td>47.44</td>
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<td>Level of education</td>
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<td>49.15</td>
<td>157</td>
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<tr>
<td></td>
<td>11–13</td>
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<td></td>
<td>( \geq 14 )</td>
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<td>20.94</td>
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<tr>
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<td>Widow/widower</td>
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<tr>
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<td>Yes</td>
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<td>Body mass index (kg/m²)</td>
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<tr>
<td></td>
<td>( \geq 30 )</td>
<td>156</td>
<td>66.67</td>
<td>159</td>
</tr>
</tbody>
</table>

NS: not significant.

* Family history of diabetes refers to first-degree relatives.

3. Results

The demographic characteristics of the study cases and controls are shown in Table 1. The cases had significantly lower levels of education and higher BMI scores compared with the controls. Also, more controls did not have a first-degree relative with a family history of diabetes compared with the cases.

Smoking was assessed according to smoking habits, duration of smoking, number of cigarettes smoked per day, number of pack-years as a smoker and smoking cessation. Univariate regression showed that current smokers had a two-fold higher risk of type 2 diabetes than non-smokers (crude OR = 2.29; 95% CI 1.26–4.16). A dose–response relationship was also found between risk of the disease and smoking habits (trend \( p = 0.003 \)). A family history of diabetes, BMI, waist circumference, plasma TG and education levels were retained in multivariate logistic-regression models as confounders because their inclusion changed the value of the OR by more than 10% in any exposure category.

Data from the multivariate logistic regression showed a relationship between type 2 diabetes and smoking (Table 2). After adjusting for a family history of diabetes and BMI, it was found that the excess risk of type 2 diabetes because of smoking habits changed a little, but remained significant. After further controlling for a family history of diabetes, BMI, waist circumference, plasma TG and education, we found a two-fold increased risk of type 2 diabetes for current smokers (OR = 3.01; 95% CI 1.57–5.75) vs. non-smokers. Significant dose–response relationships were found between smoking habits and the risk of type 2 diabetes, and the duration of smoking was also associated with a higher risk of the disease. Those who had smoked for 20–39 years had about twice the risk of having the disease (crude OR = 1.98; 95% CI 1.09–3.57) while, in those who had smoked for more than 40 years, the risk of type 2 diabetes was three times higher (OR = 3.24; 95% CI 1.68–6.31) than in non-smokers. There was a significant dose–response relationship between risk of the disease and duration of smoking (trend \( p < 0.0001 \)). After controlling for possible confounders, an association was found between the disease and duration of smoking (OR = 2.47; 95% CI 1.03–5.93 for those who smoked for 40 years or more vs. non-smokers). In addition, there was a significant dose–response relationship between risk of the disease and duration of smoking (trend \( p = 0.017 \)).

The number of cigarettes smoked per day also had an impact on the risk of type 2 diabetes. Univariate regression showed that those who smoked 10 and more cigarettes per day had nearly three times the risk of type 2 diabetes than did non-smokers (crude OR = 3.28; 95% CI 1.04–9.91). The dose–response relationship between risk of disease and number of cigarettes smoked per day was significant (trend \( p = 0.0001 \)). After adjusting for a family history of diabetes and BMI, the excess risk for type 2 diabetes due to the number of smoked cigarettes per day changed a little, but was still significant. However, after further adjustments for waist circumference, plasma TG and education levels, the relationship between type 2 diabetes and number of cigarettes smoked per day became non-significant.

The index of cumulative smoking assessed by pack-years showed an increased risk of diabetes. Current smokers who had smoked for over 10 pack-years had a three-fold higher risk of type 2 diabetes than did non-smokers (crude OR = 3.00; 95% CI 1.76–5.11), and the dose–response relationship between risk
of the disease and pack-years was significant (trend $p = 0.001$). After adjusting for a family history of diabetes and BMI, the excess risk for type 2 diabetes because of the number of pack-years changed a little, but remained significant. After further adjustments for waist circumference, plasma TG and education levels, we found that those who had smoked for 10 or more pack-years had twice the risk of diabetes (OR = 2.17; 95% CI 1.07–4.40) compared with non-smokers, and the dose–response relationship between the risk of disease and duration of smoking was significant (trend $p = 0.041$). A higher risk of diabetes was also found for ex-smokers. Univariate regression showed that those who had given up smoking less than 19 years ago still had a three-fold higher risk of type 2 diabetes than did non-smokers (crude OR = 2.96; 95% CI 1.20–7.33). After adjusting for a family history of diabetes and BMI, the extra risk of type 2 diabetes with smoking cessation changed a little, but remained significant. However, after controlling for a family history of diabetes, BMI, waist circumference, plasma TG and education, the relationship between smoking cessation and type 2 diabetes was not significant.

4. Discussion

The present study has demonstrated an increased risk of type 2 diabetes with cigarette-smoking. Indeed, current smokers had twice the risk of the disease than did non-smokers. Other prospective studies have shown similar results. Manson et al. [12], who studied 21,068 American male physicians (aged 40–84 years) for an average of 12 years in the Physicians’ Health Study, found that, compared with never-smokers, past and current smokers of less than 20 or more than 20 cigarettes per day, both demonstrated significantly increased risks of self-reported diabetes, with a dose–response relationship seen between increases in smoking and risk of diabetes. Nakashishi et al. [13] found that the multivariate-adjusted relative risk (RR) for type 2 diabetes compared with never-smokers was 3.02 (95% CI 1.15–7.94) for men who smoked 21–30 cigarettes per day and 4.09 (95% CI 1.62–10.29) for those who smoked 31 or more cigarettes per day. Wannamethee et al. [14], who studied 7735 men (aged 40–59 years) in the British Regional Heart Study, found that cigarette-smoking was associated with an increased risk of diabetes even after adjusting for confounders. However, a dose–response relationship was not observed in this cohort. In a comparatively rare study of women, Rimm et al. [15] investigated the relationship between baseline smoking and incidence of diabetes among 114,247 female nurses in the Nurses’ Health Study who were initially free of diabetes, cardiovascular disease and cancer. The RR of diabetes was 1.42 in women who smoked more than 25 cigarettes per day compared with never-smokers [15]. These results indicated that current smokers had an increased risk of type 2 diabetes.

Foy et al. [16] studied 906 subjects who were free of diabetes and found that, after multivariable adjustments, current smokers of more than 20 pack-years with normal glucose tolerance had an increased incidence of diabetes compared with never-smokers (OR = 5.66; 95% CI 2.07–15.49). Nakashishi et al. [13] found that the respective multivariate-adjusted RR for type 2 diabetes compared with never-smokers was 4.18 (95% CI 1.66–10.50) in men with a cumulative lifetime smoking exposure of 40.1 or more pack-years. In our study, we also found an association between pack-years of smoking and the incidence of diabetes. However, Wannamethee et al. [14] found no such relationship in their study.

In a systematic review and meta-analysis of studies of active smoking and the incidence of type 2 diabetes, Willi et al. [17]...
found that active smoking was associated with an increased risk of the disease. The risk was greater for heavy smokers (more than 20 cigarettes per day; RR = 1.61; 95% CI 1.43–1.80) than for those who smoked less (RR = 1.29; 95% CI 1.13–1.48), and was even lower for former smokers (RR = 1.23; 95% CI 1.14–1.33) compared with active smokers, results consistent with a dose–response phenomenon.

Nevertheless, the mechanisms that might explain the link between smoking and diabetes are not yet known. Smoking acutely impairs glucose tolerance and insulin sensitivity, raises serum cholesterol and TG levels, and increases blood pressure and heart rates [18,19]. Smoking may contribute to the development of diabetes through alterations in body-fat distribution [15], which is associated with insulin resistance [20–22], raised plasma glucose concentrations and diabetes [6]. Experimental findings suggest that smoking causes insulin resistance [23,24], an effect that might be due to nicotine stimulation of the sympathetic nervous system. Indeed, long-term use of nicotine-containing chewing gum has been associated with insulin resistance [25], and other studies have also indicated that administration of nicotine induces insulin resistance [18,26,27].

Eliasson et al. [28] have reported that smokers display typical features of the so-called insulin resistance syndrome, and that the degree of insulin resistance and extent of related metabolic abnormalities are strongly associated with smoking habits. Smoking may also lead to impaired endothelial function [29,30], which may result in reduced insulin sensitivity. Furthermore, smoking increases oxidative stress [31], which has been implicated in the development of diabetes [32]. Moreover, cigarettes contain multiple noxious substances besides nicotine such as cadmium, which is also linked to an increased risk of diabetes [33]. In rats and mice, cadmium damages pancreatic beta cells, reduces glucose tolerance and is diabetogenic [34]. Schwartz et al. [33] investigated the links between urinary cadmium and impaired fasting glucose and diabetes, and suggested that cadmium may have similar effects in humans. Will et al. [35] 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. A decreased risk of diabetes with each passing year since stopping smoking was also observed in the British Regional Heart Study [14]. However, Bezaiud et al. [36] could find no such association between smoking cessation and the risk of diabetes, and our data even show an increased risk of type 2 diabetes despite smoking cessation, although the increase was not statistically significant. However, smoking cessation has been shown to increase insulin sensitivity and improve the lipoprotein profile, despite modest increases in weight [37]. This suggests that the smoking-related risk of diabetes is reversible in those who quit the habit [14]. 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 [38]. Indeed, stopping smoking can increase life expectancy even in those who quit the habit after the age of 65 years [39]. To reduce the burden of illness due to smoking, health professionals need to encourage stopping smoking.

The present study has some limitations that need to be acknowledged. The first is related to the known fact that, in Lithuania, the quality of tobacco was stronger and less clean 20 years ago, but has changed to being less potent and cleaner over the past decade. The second limitation is the lack of data concerning people who smoke cigarettes with and without filters; these proportions were unknown in the past. We also took into account neither the strength of the cigarettes being smoked by our study subjects nor the possible impact of exposure to passive smoking.

5. Conclusion

Our data confirm that smoking may be an independent risk factor for the development of type 2 diabetes.

References


