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Smoking and diabetes in Chinese men

G T C Ko, J C N Chan, L W W Tsang, J A J H Critchley, C S Cockram

Department of Medicine and Therapeutics, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong
G T C Ko
J C N Chan
L W W Tsang
J A J H Critchley
C S Cockram

Correspondence to:
Dr Ko
gtc_ko@hotmail.com

Abstract
Smoking is a major cardiovascular risk factor and cause of death. Diabetes mellitus is also associated with an increased mortality and morbidity. Evidence concerning whether smoking increases the incidence of diabetes remains conflicting. Glycaemic status and smoking habits were analysed in 3718 Chinese subjects in order to assess the possible association between smoking and risk of diabetes in the Chinese population. The World Health Organisation 1998 criteria were used for the diagnosis of glucose intolerance. Smoking was defined as current cigarette smoking or ex-smoking without regard to daily consumption. The smoking habits of the studied subjects were correlated with glycaemic status. There were 3003 (80.8%) women and 715 (19.2%) men. The mean age (SD) was 38.4 (12.8) years (median 35.0, range 12–88 years). Of the 3718 subjects, 786 (21.1%) had diabetes, 708 (19.1%) had impaired glucose tolerance, and 2224 (59.8%) had normal results. Of the 3003 women, only 87 (2.9%) were smokers. The female smokers were younger, heavier, and had higher alcohol consumption than non-smokers. The prevalence of diabetes was similar between female smokers and non-smokers after adjustment for age, body mass index, family history of diabetes, and alcohol. Of the 715 men, 175 (24.5%) were smokers. The male smokers were younger, had lower blood pressure, and higher alcohol consumption. After adjustment for age, body mass index, family history of diabetes and alcohol, the male smokers had lower blood pressure, higher one hour plasma glucose, and more diabetes. Using logistic regression analysis (stepwise forward) with age, body mass index, alcohol, smoking, and family history of diabetes as independent variables to predict the risk of having diabetes, age and body mass index are independently associated with diabetes in both men and women. In addition, smoking is independently associated with the risk of diabetes in men, the odds ratio (95% confidence interval, CI) being 1.705 (1.106 to 2.630). Family history of diabetes is independently associated with the risk of diabetes in women, and the odds ratio (95% CI) is 1.643 (1.314, to 2.053). In conclusion, it was found that smoking is independently associated with diabetes after adjustment for age, body mass index, alcohol, and family history of diabetes in Hong Kong Chinese men, the odds ratio being 1.7. The prevalence of smoking in Hong Kong Chinese women is low and its association with diabetes is inconclusive.
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Keywords: smoking; diabetes mellitus; Chinese men

Smoking is a major cardiovascular risk factor and cause of death.[1–4] Environmental tobacco smoke exposure alone has also been reported to be associated with an increased risk of ischaemic heart disease.[5] Diabetes mellitus is also associated with an increased mortality and morbidity.[6 7] However, whether smoking increases the incidence of diabetes remains controversial. Several earlier prospective studies showed no relationship between smoking and risk of diabetes.[8 9] More recently, however, evidence has accrued suggesting a positive association between smoking and the risk of diabetes in both men and women.[10–12] These reports are confined to white people, with the exception of one study from Japan.[13] There is no information for the Chinese population.

In this study, we examine 3718 Hong Kong Chinese subjects who underwent 75 g oral glucose tolerance tests (OGTTs) for screening for diabetes, and analyse glycaemic status with smoking habits in order to assess the association between smoking and risk of diabetes.

Subjects and methods
The results of 75 g OGTTs performed in 3718 Hong Kong Chinese subjects were examined and correlated with smoking habit. These subjects had known risk factors for glucose intolerance and were referred to the Diabetes and Endocrine Center of the Prince of Wales Hospital to be screened for diabetes. The risk factors for glucose intolerance included a positive family history of diabetes, a history of gestational diabetes mellitus, obesity, and a previous history of impaired glucose tolerance. The test was performed after three days of normal carbohydrate intake and physical activity and after eight hours of fasting. No smoking was allowed during the test. Fasting, one hour, and two hour plasma glucose were measured during the OGTT. Glycated haemoglobin (HbA_{1c}) was also measured.

The newly proposed World Health Organisation consultation 1998 criteria were used for the diagnosis of glucose intolerance.[14] Subjects with fasting plasma glucose $\geqslant 7.0$ mmol/l and/or a two hour glucose $\geqslant 11.1$ mmol/l had

Table 1 Clinical characteristics of the 3718 Hong Kong Chinese subjects

	All subjects (n=3718)	Women			Men		
		All women (n=3003)	Non-smoker (n=2916)	Smoker (n=87)	All men (n=715)	Non-smoker (n=540)	Smoker (n=175)
Age (years)	38.4 (12.8)	36.7 (11.7)###	36.8 (11.7)*	33.9 (10.4)	45.3 (14.9)	46.2 (15.7)**	42.5 (11.5)
BMI (kg/m^2)	24.8 (4.3)	24.7 (4.1)#	24.7 (4.1)*	25.8 (5.0)	25.1 (5.0)	25.0 (4.6)	25.4 (5.9)
Blood pressure (mm Hg)							
Systolic	117 (17)	116 (16)##	116 (16)	116 (18)	128 (20)	130 (21)***	121 (17)
Diastolic	75 (11)	74 (10)###	74 (10)	72 (10)	80 (13)	81 (13)***	76 (11)
Plasma glucose (mmol/l)							
Fasting	5.6 (1.8)	5.6 (1.7)	5.6 (1.7)	5.6 (2.2)	5.9 (1.9)	5.9 (1.9)	5.9 (2.1)
1 hour	10.6 (4.1)	10.3 (4.0)	10.3 (3.9)	10.6 (4.6)	11.7 (4.6)	11.6 (4.6)**	12.2 (4.6)
2 hour	8.3 (4.5)	8.1 (4.3)	8.1 (4.3)	8.1 (4.4)	9.2 (5.1)	9.2 (5.1)	9.4 (4.9)
HbA$_{1C}$ (%)	5.92 (1.07)	5.83 (1.02)###	5.83 (1.00)	5.87 (1.41)	6.31 (1.22)	6.28 (1.23)	6.37 (1.17)
AUC-PG (mmol/hour/l)	17.5 (6.9)	17.1 (6.6)	17.1 (6.6)	17.5 (7.6)	19.3 (7.7)	19.1 (7.7)**	19.9 (7.7)
% (No) smoking	7.0 (262)	2.9 (87)###	0	100	24.5 (175)	0	100
% (No) alcohol drinking	4.7 (174)	1.2 (37)###	0.7 (1.9)***	20.7 (18)	19.2 (137)	9.8 (53)***	48.0 (84)
% (No) FH of diabetes	47.4 (1761)	46.0 (1380)	45.4 (1324)***	64.4 (56)	53.2 (381)	46.6 (252)***	73.7 (129)
% (No) normal OGTT	59.8 (2224)	62.5 (1876)	62.3 (1818)	66.7 (58)	48.7 (348)	49.6 (268)*	45.7 (80)
% (No) IGT	19.1 (708)	19.4 (583)#	19.5 (569)	16.1 (14)	17.5 (125)	18.0 (97)	16.0 (28)
% (No) diabetes	21.1 (786)	18.1 (544)##	18.1 (529)	17.2 (15)	33.8 (242)	32.4 (175)*	38.3 (67)

Mean (SD) or percentage (number).
BMI: body mass index, FH: family history, HbA$_{1C}$: glycated haemoglobin, OGTT: oral glucose tolerance test, AUC-PG: area under curve of plasma glucose in the OGTT, IGT: impaired glucose tolerance.
p Values: smokers v non-smokers: *<0.05, **<0.01, ***<0.001 after adjustment for age, BMI, alcohol, and family history of diabetes if appropriate; men v women: #<0.05, ##<0.01, ###<0.001 after adjustment for age, BMI, smoking, and alcohol if appropriate.

diabetes, those with fasting glucose <7.0 mmol/l and two hour glucose ≥7.8–11.1 mmol/l had impaired glucose tolerance, and those with fasting glucose <7.0 mmol/l and two hour glucose <7.8 mmol/l had normal glucose tolerance. Smoking (and drinking) is defined as current cigarette smoking (or current alcohol drinking) or ex-smoking (ex-drinking) irrespective of the daily number of cigarettes (or amount of alcohol) consumed.

Plasma glucose was measured by a glucose oxidase method (Diagnostic Chemicals reagent kit). Both the intra-assay and interassay coefficients of variation for glucose were 2% at 6.6 mmol/l. HbA$_{1c}$ was measured by an automated ion exchange chromatographic method (Bio-Rad Laboratory, Hercules, CA, USA; manufacturer's reference range 5.1%–6.4%). The interassay and intra-assay coefficient of variation for HbA$_{1c}$ was ≤3.1% at values below 8.5%.

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS (version 7.5) software on an IBM compatible computer. All results are expressed as mean (SD) or percentage (number) where appropriate. Area under the curve of the plasma glucose (PG) in the OGTT (AUC-PG) is defined as [1 hour PG + (fasting PG + 2 hour PG)/2]. The Student's t test and χ^2 tests were used for two group comparisons where appropriate. The analysis of covariance was used for between group comparisons with age, body mass index, alcohol, family history of diabetes, and/or smoking as covariates where appropriate. Logistic regression analysis (stepwise forward) using age, body mass index, alcohol, smoking, and family history of diabetes as independent variables was performed to estimate their independent effects on the risk of having diabetes. Odds ratio with 95% confidence intervals of having diabetes in smoking subjects was computed. A p value <0.05 (two tailed) was considered to be significant.

Results

There were 3718 subjects of whom 3003 (80.8%) were women and 715 (19.2%) men. There were many more women than men as a history of gestational diabetes, which is confined to women, was one of the major indications for OGTT screening in the studied subjects. The mean (SD) age was 38.4 (12.8) years (median 35.0, range 12–88 years). Their clinical characteristics and biochemical parameters are summarised in table 1. Of the 3718 subjects, 786 (21.1%) had diabetes, 708 (19.1%) had impaired glucose tolerance, and 2224 (59.8%) had normal glucose tolerance. Compared with women, men were older, more obese, and were more likely to smoke (24.5% v 2.9%, p<0.001) and drink alcohol (19.2% v 1.2%, p<0.001). Systolic and diastolic blood pressure, HbA$_{1c}$, and prevalence of diabetes were also higher in men than women after adjustment for age, body mass index, smoking, and alcohol (table 1).

Of the 3003 women, only 87 (2.9%) were smokers. The female smokers were younger, more obese, and had higher prevalence of alcohol drinking than non-smokers (table 1). The prevalence of diabetes was similar between female smokers and non-smokers after adjustment for age, body mass index, family history of diabetes, and alcohol (table 1). Women with a past history of gestational diabetes (n=1009) had similar smoking rates to those who had no past history of gestational diabetes (n=1994) (3.6% v 2.5%, p=0.063).

Of the 715 men, 175 (24.5%) were smokers. The male smokers were younger and were more likely to drink alcohol than non-smokers (table 1). After adjustment for age, body mass index, family history of diabetes and alcohol, the male smokers had lower blood pressure, higher one hour plasma glucose, AUC-PG, more diabetes, and were less likely to have normal glucose tolerance (table 1).

Table 2 summarises the logistic regression analysis (stepwise forward) with age, body mass index, alcohol, smoking, and family

Table 2 Logistic regression analysis (stepwise forward) using age, body mass index (BMI), alcohol, smoking, and family history of diabetes as independent variables accounting the risk of having diabetes

Independent variables	β	SE	p Value	Odds ratio (95% CI)
Women (n=3003) (Nagelkerke R^2=0.085)				
Age	0.058	0.004	<0.001	1.059 (1.051 to 1.068)
BMI	0.090	0.013	<0.001	1.094 (1.067 to 1.122)
Family history of diabetes	0.489	0.114	<0.001	1.643 (1.314 to 2.053)
Men (n=715) (Nagelkerke R^2=0.142)				
Age	0.041	0.007	<0.001	1.042 (1.027 to 1.057)
BMI	0.063	0.021	0.003	1.065 (1.022 to 1.109)
Smoking	0.534	0.221	0.016	1.705 (1.106 to 2.630)

CI = confidence interval.

history of diabetes as independent variables to predict the risk of having diabetes. Age and body mass index are independently associated with diabetes in both men and women. After adjustment for age, body mass index, alcohol and family history of diabetes, smoking is significantly associated with the risk of diabetes in men, and the odds ratio (95% confidence interval, CI) is 1.705 (1.106 to 2.630). Family history of diabetes is associated with risk of diabetes in women after adjustment for age, body mass index, smoking and alcohol, and the odds ratio (95% CI) is 1.630 (1.303 to 2.309).

Discussion

Information on the correlation between cigarette smoking and risk of diabetes is limited. Three studies among white people report a 1.4–3.3 times higher risk of diabetes among men or women who smoked 20–25 or more cigarettes per day compared with those who had never smoked.[10–12] However, another three studies show negative findings.[8 9 15] Information among the Asian population is scanty. One recent report among Japanese men showed that those who were currently smoking 16 or more cigarettes per day had a 3.2 times higher risk of developing type 2 diabetes compared with those who had never smoked.[13] In the present analysis, we found a positive independent association with an odds ratio of 1.7 between smoking and risk of diabetes in Chinese men. There was no statistical significance in women due to the very low smoking rates and little difference in the diabetic rates between smokers and non-smokers (17.2% *v* 18.1%). With the present sample size of ~3000 women, the power of the study was calculated to be as low as 0.15 and the false negative rate (type 2 statistical error) 85%.

Our study has several limitations. First of all, the subjects have known risk factors for glucose intolerance, and they were recruited into the study for outpatient OGTT screening. Also we have excluded those patients who presented with severe metabolic decompensation. Our group has previously reported the prevalence of smoking in Hong Kong on a population based sample[16]: 22.9% in men and 1.8% in women. These are similar to those reported in this study (24.5% in men and 2.9% in women). So although our subjects are selected, there should be minimal bias on their smoking habits. Another limitation of our study is the low prevalence of smoking in female subjects, which may account for the insignificant results among females. We have previously reported a

low smoking prevalence among Chinese women.[16 17] A third limitation of our study is the lack of detail on the quantity of cigarettes smoked. Feskens and Kromhout[10] and Rimm *et al*[11 12] reported up to a 3.3 times higher risk of diabetes in heavy smokers (20 or more cigarettes per day) compared with non-smokers. Kawakami *et al* also reported a 3.2 times higher risk of developing diabetes in Japanese men who were smoking 16 or more cigarettes per day.[13] Those who smoked fewer than 16 cigarettes per day showed a higher but insignificant risk of diabetes compared with non-smokers.[13] Our study showed an odds ratio of 1.7 of smoking (current or ex-smokers) on the risk of diabetes. This figure is similar to that reported by Simon *et al* who found that among 9435 elderly non-black women, smokers of 10 or more cigarettes per day had an odds ratio of 1.38 compared with never smokers.[18] Our result may be underestimated because of attenuation by including those who smoke but not heavily. In addition, the smoking habit is self reported and this may have potential bias on the accuracy of the data. Ideally, an objective measure of smoking such as expired carbon monoxide or blood carboxyhaemoglobin levels will be helpful in confirming smoking status. This kind of information is not available in this study, however, because of resource limitation.

It has been confirmed that cigarette smoking causes a transient increase in plasma glucose concentrations.[19–21] Chronic exposure to smoking may hence induce a glucose intolerant state. Smoking is one of the most important cardiovascular risk factors in both diabetic and non-diabetic subjects.[22] Stopping smoking could be the most cost effective intervention to reduce risk of coronary heart disease,[23] and the finding of increased risk of developing diabetes in smokers further emphasised the importance of this.

Smoking has been reported to cause an acute increase in blood pressure.[24] However, many epidemiological studies reported a lower blood pressure level in smokers than in non-smokers.[25 26] In this study, we also noted a significantly lower blood pressure in Chinese male smokers compared with non-smokers. The association between smoking and blood pressure is still elusive. Benowitz and Sharp reported a significant inverse correlation between serum cotinine (the major metabolite of nicotine) and systolic and diastolic blood pressure.[27] On the other hand, in a longitudinal study, Charlton and While found that lower blood pressure at age 10 was related to the onset of smoking in children at age 16.[28] This suggested the possibility that low blood pressure might precede the onset of smoking. More research is needed on the relationship between smoking and blood pressure.

In conclusion, we found that smoking is independently associated with development of diabetes after adjustment for age, body mass index, alcohol, and family history of diabetes in Hong Kong Chinese men, and the odds ratio is 1.7. The prevalence of smoking in Hong Kong

Chinese women is low and its association with diabetes is still inconclusive.

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