

Research Article

# Type 2 Diabetes Mellitus and Habits Lifestyle Increases the Risk of Cervical Cancer: a Cross-Sectional Population-Based Study

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## Abstract

**Background:** Timely detection allows the inclusion of vulnerable populations into the cervical cancer (CC) screening programs, particularly in low- and middle-income countries. The aim was determine both the prevalence and the risk of CC in patients who have type 2 diabetes mellitus (T2DM).

**Methods:** A cross-sectional population-based survey in Mexico was conducted using a probabilistic, multistage, and stratified cluster sampling design. The structured questionnaire included information on geographic region, personal history, and life styles, and anthropometric measures. A total of 160 cases of CC (median age 48 years, range 24-81) and 25,262 control females (median age 39 years, range 20-99) were included.

**Results:** The prevalence of CC in women with T2DM was significantly higher compared with females without diabetes (1,336 vs. 576 subjects per 100,000 inhabitants,  $p < 0.001$ ). In all univariate (U) and multivariate (M) logistic regression models (LRM), the ORs for CC displayed a significant association with diabetes (ULRM OR=2.338; 95% CI 1.511-3.618,  $p < 0.001$ , MLRM1 OR=2.098; 95% CI 1.345-3.272,  $p = 0.001$ , MLRM2 OR=1.719; 95% CI 1.0.33-2.862,  $p = 0.001$ ) and tobacco smoking (ULRM OR=1.979; 95% CI 1.368-2.863,  $p < 0.001$ , MLRM1 OR=1.847; 95% CI 1.234-2.765,  $p = 0.003$ , MLRM2 OR=1.859; 95% CI 1.191-2.902,  $p = 0.006$ ). The ULRM indicated a significant association for separate (OR=1.906; 95% CI 1.178-3.085,  $p = 0.009$ ), widowed (OR=1.615; 95% CI 1.059-2.462,  $p = 0.026$ ) and single MS (OR=3.297; 95% CI 1.618-6.717,  $p = 0.001$ ). The MLRM2 indicated a similar association for the variables sedentary (OR=8.676; 95% CI 1.204-62.497,  $p = 0.032$ ), physical activity (OR=0.115; 95% CI 0.016-0.827,  $p = 0.032$ ) and body fat percentage (OR=1.084; 95% CI 1.023-1.149,  $p = 0.006$ ).

**Conclusion:** This study supports an association between personal history of diabetes and tobacco smoking and life styles with CC.

**Keywords:** Cervical cancer; Diabetes; Risk factors; Logistic regression; Lifestyle characteristics; Sociodemographic components

## Introduction

Diabetes and cancer are two common non-communicable chronic diseases that have an enormous impact on worldwide health and the economy [1], and they are a considerable public health problem. Diabetes Mellitus (DM) affects more than 100 million people around the world [2]. Several studies have reported that people with diabetes have a significantly higher risk of many forms of cancer [1]. In addition, diabetes is associated with an increased risk of total cancer mortality [3-8] and with site-specific mortality from cancer of the endometrium [9,10], breast [10-14], colorectum [10,15-18], pancreas [10,19-22], liver [10,23-25], and prostate [26-29]. Moreover an association between abnormal glucose tolerance and the risk of cancer mortality has also been demonstrated for Western countries [30-32]. Recently, several studies reported a direct association between various cancers [33], including cervical cancer [34], and with both Metabolic Syndrome (MetS) and individual components of MetS [33-42]. Several epidemiologic studies have reported diabetes as a risk factor for endometrial cancer, independent from obesity [41,43-46]. Studies conducted in the United State of America, Canada and Spain has revealed that women with diabetes undergo mammography and Papanicolaou (paP) smear procedures less frequently than women without diabetes [46-51]. In addition, one study in Mexico reported a direct association between both low-grade cervical lesions and infection with human papilloma virus type

1 with glucose concentration [52]. Given the substantial increase of both non-communicable chronic diseases such as diabetes mellitus and the high prevalence of cervical cancer, there is a great interest in determining susceptible populations and cofactors that could increase the mortality and the risk of cervical cancer; additionally there are limited information about the relationship of type 2 DM (T2DM) and cervical cancer. Therefore the aim of the present study was to determine both the prevalence and the risk of cervical cancer among women with diabetes.

## Material and Methods

### Study design, data collection and participants

A cross-sectional population-based survey from Mexico was conducted from October 2005 to May 2006. The survey includes data from 48 304 households [53-55] of urban ( $\geq 2$  500 inhabitants) and rural ( $< 2$  500 inhabitants) geographic regions of Mexico [53-55]. Sociodemographic and personal health questionnaires, lifestyles habits and blood pressure were obtained from all participants. For the present study, only the data from adult women were selected. A total of 25, 422 women (median age 39, range 20-99) were included. However, because in the survey the response rates for anthropometric measurements were 79.6%, the associated analysis between cervical cancer and anthropometric measurements was reported in a previous publication [56], which included 20,236 women. Height was measured to the nearest 0.1 cm using a stadiometer, and body weight

was measured using a digital scale [53,54]. Body mass index (BMI) was calculated according to Quetelet's index ( $\text{kg}/\text{m}^2$ ), and the body fat percentage (BFP) was obtained using the Deurenberg equation [ $\text{BFP} = 1.2(\text{BMI}) + 0.23(\text{age}) - 10.8(\text{sex}) - 5.4$ ]. Waist circumference (WC) was measured at the midpoint between the highest part of the iliac crest and the lowest part of the rib margin of the median axial line [53,54].

### Survey instrument

The National Survey of Health and Nutrition 2006 (ENSANUT 2006; Encuesta Nacional de Salud y Nutrición 2006, for its acronym in Spanish) had a probabilistic, multistage, stratified cluster sampling design. The structured questionnaire included information on sociodemographic characteristics such as geographic region, literacy and marital status. In addition, the instrument also included personal history of type 2 diabetes mellitus (T2DM) and cervical cancer; lifestyle habits, such as tobacco smoking, alcohol consumption, physical activity, sedentary habits; and anthropometric measures.

### Ethical review

The protocol was approved by the Research, Ethics and Biosecurity committees of the National Institute of Public Health [53-55]. All participants signed an informed letter of consent after receiving an explanation of the nature, objectives and the risks inherent to the study [53-55].

### Statistical analysis

Categorical variables were described by both the absolute frequency and percentage and the corresponding 95% confidence interval (CI). All categorical variables were compared using a Yates corrected chi square test. The continuous variables from the different groups were compared by the Mann-Whitney U and Student's t tests. The rates of specific prevalence for cervical cancer in patients with diabetes and the crude odds ratios (ORs) were calculated. To estimate the association of cervical cancer with sociodemographic characteristics, literacy, marital status, T2DM and lifestyle habits, both univariable and multivariable logistic regression analysis was used to obtain the ORs and their corresponding 95% CIs. The same method was used when including anthropometric measurements in the regression model. Thus, two multivariate regression models were calculated: one model without anthropometric measurements and an additional model that included these measures. A p value < 0.05 (2-sided testing) was considered significant.

## Results

A total of 160 cases of cervical cancer (median age 48 years, range 24-81) and 25,262 control females (median age 39 years, range 20-99) were included. Table 1 expresses the distribution of cases for cervical cancer and controls in relation to selected sociodemographic and lifestyle characteristics. The prevalence of cervical cancer was similar in women who lived in rural, urban and metropolitan areas.

The prevalence rate of cervical cancer in women with T2DM (1,336 subjects per 100,000 inhabitants) was significantly higher ( $p < 0.001$ ) than their counterparts without diabetes (576 subjects per 100,000 inhabitants), and their risk is twice as high (OR=2.34; CI 95% 1.47-3.68,  $p = 0.0001620$ ). On the other hand, the averages for weight, BMI and WC were calculated only for 20,236 women and had

**Table 1:** General, sociodemographic, lifestyle, and clinical characteristics of the study population.

Variables	Total N=25422	Non-cervical cancer n=25262 n, (%; 95% CI)	Cervical cancer n=160 n, (%; 95% CI)	p Value
Rural	6666	6626 (26.2; 25.7-26.8)	40 (25; 18-32)	NS
Urban	7355	7311 (28.9; 28.4-29.5)	44 (28;21-34)	NS
Metropolitan	11401	11325 (44.8; 44.2-45.4)	76 (48; 40-55)	NS
Literacy	22243	22110 (87.5; 87.1-87.9)	133 (83; 77-89)	NS
Free union	3261	3237 (12.8; 12.4-13.2)	24 (15; 09-21)	NS
Married	13430	13353 (52.9; 52.2-53.5)	77 (48; 40-56)	NS
Separate	1687	1668 (6.6; 6.3-6.9)	19 (12; 07-17)	0.012
Divorced	548	542 (2.1; 2.0-2.3)	6 (4; 1-7)	NS
Widower	2736	2710 (10.7; 10.3-11.1)	26 (16; 11-22)	0.034
Single person	3743	3735 (14.8; 14.3-15.2)	8 (5; 2-8)	0.001
Sedentary	1436	1430 (5.7; 5.4-5.9)	6 (4; 1-7)	NS
Physical activity	23986	23832 (94.3; 94.1-94.6)	154 (96; 93-99)	NS
Tobacco smoking	3370	3333 (13.2; 12.8-13.6)	37 (23; 17-30)	<0.001
Alcohol drinking	6699	6649 (26.3; 25.8-26.9)	50 (31; 24-38)	NS
Diabetes mellitus	1797	1773 (7.0; 6.7-7.3)	24 (15; 09-21)	<0.001

\*BMI, body mass index; WC, waist circumference; BFP body fat percentage

a similar distribution between the cases and controls [56] (for a total of 131 cases: weight  $67.42 \pm 13.43$ , BMI  $29.04 \pm 5.13$  and WC  $95 \pm 12$ ; for 20,105 controls: weight  $66.49 \pm 14.27$ , BMI  $28.59 \pm 5.63$  and WC  $93 \pm 13$ ). However, the BFP was higher ( $p=0.012$ ) in females with cervical cancer ( $n=131$ ,  $40 \pm 7$ ) than in women without cancer [56] ( $n= 20,105$ ,  $39 \pm 8$ ).

Table 2 shows the OR analysis and the corresponding 95% CIs. The estimated ORs for cervical cancer, in both logistic regression models, display a significant direct association only for diabetes and tobacco smoking, but the univariate regression model indicated a similar significant association for diabetes, tobacco smoking, and for three marital statuses: separate, widowed and single person.

Table 3 provides details on an additional multivariate logistic regression model that included the anthropometric measures. The OR analysis revealed a significant association between cervical cancer and diabetes mellitus, sedentary, physical activity, tobacco smoking and body fat percentage.

Table 4 shows the distribution of the selected sociodemographic and lifestyle characteristics for diabetic patients. According to the analysis, the prevalence of all selected characteristics is similar in diabetic women with and without cervical cancer. In the same manner, the percentage of people with life styles changes such as dietary ( $n=387/1773$ , 21.83%; CI 95% 19.90-23.75 vs.  $n=4/24$ , 16.67%; CI 95% 1.76-31.58) and physical activity ( $n=106/1773$ , CI 95% 5.98; 4.87-7.08 vs.  $n=1/24$ , 4.17; CI 95% -3.83-12.16) modifications and pharmacological treatment ( $n=1498/1773$ , 84.49%; CI 95% 82.80-86.17 vs.  $n=21/24$ , 87.50%; CI 95% 74.27-100) was similar. However, the percentage of women that use herbal and natural remedies was higher in diabetic patients with cervical cancer than among their counterparts without cancer ( $n=94/1773$ , 5.30%; CI 95% 4.26-6.34 vs.  $n=5/24$ , 20.83%; CI 95% 4.59-37.08;  $p=0.008$ ).

**Table 2:** Univariate and multivariate logistic regression models (multivariate model 1).

Variables	Univariate			Multivariate		
	B	OR (CI 95%)	p Value	B	OR (CI 95%)	p Value
DM	0.849	2.338 (1.511-3.618)	<0.001	0.741	2.098 (1.345-3.272)	0.001
Rural	-0.065	0.938 (0.655-1.342)	NS	-0.037	0.963 (0.642-1.446)	NS
Urban	-0.071	0.931 (0.658-1.319)	NS	-0.086	0.917 (0.628-1.339)	NS
Metropolitan	0.107	1.113 (0.816-1.520)	NS	0.037	1.038 (0.691-1.558)	NS
Literacy	-0.353	0.702 (0.464-1.064)	NS	-0.284	0.753 (0.484-1.169)	NS
Free union	0.183	1.201 (0.777-1.856)	NS	-0.162	0.851 (0.480-1.506)	NS
Married	-0.189	0.827 (0.606- 1.129)	NS	-0.381	0.683 (0.430-1.086)	NS
Separate	0.645	1.906 (1.178-3.085)	0.009	0.188	1.206 (0.658-2.212)	NS
Divorced	0.575	1.777 (0.783-4.035)	NS	0.115	1.122 (0.453-2.779)	NS
Widower	0.479	1.615 (1.059-2.462)	0.026	0.174	1.190 (0.672-2.105)	NS
SP*	1.193	3.297 (1.618-6.717)	0.001	-0.703	0.495 (0.224-1.092)	NS
Sedentary	-0.432	0.649 (0.287-1.470)	NS	0.596	1.815 (0.794-4.148)	NS
PA*	0.432	1.540 (0.680-3.487)	NS	0.596	0.551 (0.241-1.259)	NS
TS*	0.683	1.979 (1.368-2.863)	<0.001	0.614	1.847 (1.234-2.765)	0.003
AD*	0.241	1.272 (0.910-1.780)	NS	0.094	1.099 (0.763-1.582)	NS

\* SP, single person; PA, physical activity; TS, tobacco smoking; AD, alcohol drinking

**Table 3:** Additional multivariate logistic regression model (multivariate model 2).

Variables	Multivariate analysis		
	B	OR (CI 95%)	p Value
Diabetes Mellitus	0.542	1.719 (1.0.33-2.862)	0.001
Rural	0.157	1.170 (0.724-1.892)	NS
Urban	-0.235	0.791 (0.514-1.216)	NS
Metropolitan	0.235	1.265 (0.822-1.9469)	NS
Literacy	-0.278	0.758 (0.463-1.239)	NS
Free union	0.141	1.152 (0.388-3.420)	NS
Married	-0.301	0.740 (0.265-2.067)	NS
Separate	0.433	1.557 (0.521-4.649)	NS
Divorced	0.338	1.403 (0.459-4.288)	NS
Widower	-0.321	0.725 (0.237-2.217)	NS
Single Person	-1.005	0.366 (0.106-1.270)	NS
Sedentary	2.161	8.676 (1.204-62.497)	0.032
Physical Activity	2.164	0.115 (0.016-0.827)	0.032
Tobacco Smoking	0.620	1.859 (1.191-2.902)	0.006
Alcohol Drinking	0.181	1.198 (0.803-1.787)	NS
Weight	0.009	1.009 (0.980-1.039)	NS
Body Mass Index	-0.111	0.895 (0.802-0.998)	NS
Waist Circumference	-0.000998	0.999 (0.991-1.007)	NS
Body Fat Percentage	0.081	1.084 (1.023-1.149)	0.006

## Discussion

The available data show that the major cause of cervical cancer is chronic infection, especially with the sub-types 16 and 18 of oncogenic Human Papilloma Virus [57-60] (HPV), and other viral infections and transmitted diseases also increase the prevalence of this cancer [61,62]. In both the United States of America and northern Europe,

there is evidence of a rising frequency of cervical adenocarcinoma (AC) in both absolute and relative terms [63]. The frequency of AC rises with the number of sexual partners and with a beginning sexual activity at an early age, indicating sexually transmitted (viral) factors [63]. In the present study, the percentages of people with free union, married and divorced marital statuses were identical in both groups; however, among females with cervical cancer, the proportion of cases was significantly lower in single subjects ( $p=0.001$ ) and significantly higher in subjects with a separated ( $p=0.012$ ) or widowed ( $p=0.034$ ) marital status, suggesting differential patterns of sexual activity.

On the other hand, non communicable chronic diseases are the major contributors to public health problems around the world and their incidence are increasing, particularly in low- and middle-income countries [64]. The most important diseases associated are cardiovascular disease, cancer, chronic respiratory diseases, and diabetes [64]. There are studies have reported that subjects with diabetes have a significantly associated an increased risk of stomach, colorectal, pancreatic, liver, lung, breast, endometrial, ovarian, cervical and prostate cancers compared with those without diabetes [65,66]. In a study of the Japanese population, the risk was significantly higher for cancers of the stomach, liver, lung and cervix uteri among women [67]. The association found in the present study between cervical cancer and diabetes is consistent with the findings in other populations and suggests that a personal history of diabetes should be considered a risk factor for cervical cancer [65-67]. Similarly, O'Mara et al. also revealed comparable findings that have demonstrated diabetes is a risk factor for cancer of the uterine corpus and cancer of the vulva and vagina [68].

Compared with the controls, the cases had the same prevalence of alcohol drinking; however, the prevalence of tobacco smoking was higher ( $p<0.001$ ). A personal history of tobacco smoking should be also considered as a risk factor for cervical cancer, and this association is consistent with the findings of other authors. For the treatment

**Table 4:** Distribution of sociodemographic and lifestyle characteristics for diabetic patients.

Variables	Total diabetic patients n=1797 n (%; 95% CI)	Non cervical cancer n=1773 n (%; 95% CI)	Cervical cancer n=24 n (%; 95% CI)	p Value
Rural	390 (22; 20-24)	382 (22; 20-23)	8 (33.3; 14.5-52.2)	NS
Urban	564 (31; 29-34)	559 (31; 29-33)	5 (20.8; 4.6-37.1)	NS
Metropolitan	843 (47; 45-49)	832 (47; 45-49)	11 (45.8; 25.9-65.8)	NS
Literacy	1423 (79.2; 77.3-81.1)	1407 (79; 77-81)	16 (66.7; 47.8-85.5)	NS
Free union	157 (8.7; 7.4-10)	152 (9; 7-10)	5 (20.8; 4.6-37.1)	NS
Married	938 (52.2; 4.9-5.5)	927 (52; 50-55)	11 (45.8; 25.9-65.8)	NS
Separate	146 (8; 7-9)	143 (8; 7-9)	3 (12.5; 0.0-25.7)	NS
Divorced	43 (2.4; 1.7-3.1)	43 (2; 2-3)	0 (0.0; 0.0-0.0)	NS
Widower	402 (22; 20-24)	397 (22; 20-24)	5 (20.8; 4.6-37.1)	NS
Single person	109 (6; 5-7)	109 (6; 5-7)	0 (0.0; 0.0-0.0)	NS
Sedentary	188 (10.5; 9-12)	185 (10; 9-12)	3 (12.5; 0.0-25.7)	NS
Physical activity	1609 (89.5-91)	1588 (90; 88-91)	21 (88; 74-100)	NS
Tobacco smoking	258 (14.4; 12.7-16.1)	251 (14; 13-16)	7 (29.2; 11.0-47.4)	NS
Alcohol drinking	392 (22; 20-24)	387 (22; 20-24)	5 (20.8; 4.6-37.1)	NS
Weight	68.55 ± 17.16	68.53 ± 17.22	70.44 ± 12.21	NS
BMI*	29.88 ± 6.17	29.87 ± 6.19	30.53 ± 5.16	NS
WC*	100.94 ± 18.59	100.95 ± 18.67	100.33 ± 11.93	NS
BFP*	43.32 ± 7.51	43.32 ± 7.51	43.42 ± 7.29	NS

\*BMI, body mass index; WC, waist circumference; BFP body fat percentage

of carcinoma of the cervix with primary irradiation, the five-year survival in smokers and diabetic patients was lower than nonsmokers and subjects without diabetes that had Stage I and II carcinoma of the cervix, but only patients with a history of nicotine abuse had significantly less favorable cure rates in Stages III and IV of cervical carcinoma [69]. The frequency of side effects of primary irradiation is distinctly higher in smokers than in nonsmokers [69]. In addition, cases with severe irreversible changes occurred in practically twice as many smokers than nonsmokers [69]. The injuries caused by smoking not only reduce the biological effectiveness of ionizing radiation but also increase the rate of side effects, most likely due to the deficient capacity for regeneration of the tissue surrounding the tumor [69].

Similarities with the epidemiological association between endometrial cancer and some components of metabolic syndrome based on clinical series, such as overweight, hypertension and diabetes have been reported [63]; however, for body mass index, only a trend with the increasing prevalence of cervical cancer was observed.

#### Possible molecular mechanisms for increased cervical cancer in patients with type two diabetes mellitus

The mechanisms postulated for increased cancer risk in diabetes include hyperglycemia, hyperinsulinemia with stimulation of IGF-1 axis, and obesity, as well as other factors such as increased cytokine production [65], tobacco smoking and intracellular signaling pathways. For instance, in cervical cancer cells in diabetic patients, the possible mechanism proposed involves the integrity of the LKB1-AMPK-mTOR signaling pathway [70-73]. In addition, the mTOR signaling pathway senses and responds to nutrient availability, energy efficiency, stress, hormones and mitogens to modulate protein synthesis [74]. Moreover, the role of the mTORC2 complex is mainly related to the control of Akt S473 phosphorylation and the control of

SGK activity [75], suggesting the crucial involvement of this signaling pathway in the onset and progression of diabetes and cancer [76], two of major non communicable chronic and metabolic diseases worldwide.

Some studies have reported other evidence linking cervical cancer with diabetes. Xiao X et al. demonstrated that metformin could induce both apoptosis and autophagy and thus inhibited growth in cervical cancer cells when LKB1 was expressed in specific cell lines, most likely through the integrity of the LKB1-AMPK-mTOR signaling pathway [70]. In cervical cancer cells with intact LKB1, there was improved activation of AMPK, promoting the inhibition of mTOR and prompting the sensitivity of cells to metformin [70]. In addition, both tested pharmacological AMPK activators, AICAR and A23187 exerted the anti-proliferative effect on cervical cancer cells by suppressing AMPK/mTOR signaling activity. AICAR has been widely used to suppress cancer cell growth through the activation of LKB1, and A23187 inhibits cervical cancer cell growth through activation of Ca(2+)/calmodulin-dependent protein kinase beta, another upstream kinase of AMPK [77]. Although best known for its effects on metabolism, AMPK has many other functions, including regulation of mitochondrial biogenesis and disposal and cell polarity [78]. Both tumor cells and viruses have mechanisms to down-regulate AMPK, allowing them to escape its restraining influences on growth [71].

The development of cervical cancer is a complex interaction between environmental and genetic factors such as the chronic infection with oncogenic HPV, especially sub-types 16 and 18, and cellular and molecular mechanisms that affect the physiological response of the cell, including cytokine production that can disturb the intracellular signaling pathways and genetic susceptibility that

can also affect these signaling pathways and the genetic viral variants. In Hispanic patients, a direct association between specific HLA class II haplotypes (DRB1\*1501-DQB1\*0602) with cervical carcinoma has been reporting, suggesting that these haplotypes may influence the immune response to specific HPV-encoded epitopes and affect the risk of cervical neoplasia [79]. Moreover, the additional multivariate logistic regression model (Table 3) indicated a significant association between cervical cancer and several risk factors of T2DM, such as sedentary, physical activity, tobacco smoking and one component of MetS (diabetes mellitus). Finally, this analysis demonstrated a significant association with body fat percentage, suggesting a complex interaction with similar physiopathology mechanisms. In Mexico, Berumen et al. recently demonstrated that the upregulated genes expression of CDC20, NUSAP1, and CDKN3 were associated with high-grade cervical intraepithelial neoplasia, and only CDKN3 was associated with poor survival, independent from clinical stage [80]. Two mitochondrial (mt) DNA genes (mitochondrial aspartic acid tRNA and mitochondrial lysine tRNA), the Amerindian haplogroup B2 of the polymorphism of mt-DNA D-loop, increase the risk for cervical cancer (odds ratio (OR) =1.6; 95% confidence interval (CI): 1.05-2.58) [81]. In addition, Villegas-Sepulveda et al. demonstrated that the HPV-16-positive carcinoma cells bear viral variants that contain single nucleotide polymorphisms (SNPs) in their DNA sequence, and these viral sequences are sufficient to produce heterogeneity in the splicing profile sufficient to alter the binding site of at least one splicing factor, changing the ability of splicing factors to bind the transcript [82]. Wu Y et al. demonstrated that the mt C150T polymorphism increases the risk of cervical cancer (OR=4.9, 95% CI=2.6-9.3,  $P=9.9 \times 10^{-7}$ ) as does HPV infection (OR=4.5, 95% CI=2.5-8.1,  $P=6.6 \times 10^{-7}$ ) in a Chinese population [83].

These data suggest that cervical cancer is a communicable disease but with a similar pattern of behavior to non-communicable chronic disease as characterized by multiple risk factors, including several virus variants, various patterns of infection, sociodemographic factors, lifestyle habits, personal history of chronic disease and genetic susceptibility to the infection and therapeutic response from patients.

For these reasons, determining the heterogeneity of cancer with respect to its geographical distribution, etiology, and related risk factors requires a number of cancer-specific strategies such as inclusion in cervical cancer screening programs of people susceptible to developing cervical neoplasms.

## Limits

A limit of the present study is that reported old data. However, both type 2 diabetes mellitus and cervical cancer are increasing around the world. Although there are a high number of articles about type 2 diabetes mellitus and cancer, there are limited information about the relationship of type 2 diabetes mellitus and cervical cancer. Therefore, the present study contributes to increase the knowledge of association between type 2 diabetes mellitus and cervical cancer. The critical necessity of including susceptible people is because the success of any preventive program lies in the early detection of disease. Considering diabetic patients are a susceptible population likely to develop cervical cancer, health authorities could increase the survival rates for cervical cancer and improve the quality and coverage of cancer screening by also extending their interventions in

low-resource health-care settings, particularly in low- and middle-income countries or in vulnerable areas in developed countries.

For example, Latinas in the United States have higher morbidity and mortality rates for breast and cervical cancers compared with non-Latina Whites, often because of lower screening rates [84,85]. Jandorf L et al. demonstrated that a culturally customized educational program, such as screening program, increases the detection of breast and cervical cancer among Latinas and also can decrease the morbidity and mortality rates of cervical cancer by increasing cancer early screening [84]. In addition, these activities can establish effective cancer treatment programs, such as vaccination against human papillomavirus in diabetic patients, and, as a consequence, reduce cervical cancer treatment costs.

## Conclusion

The present study demonstrates that a personal history of diabetes and tobacco smoking and life style factors are associated with cervical cancer. These findings suggest that all these features could be considered as potential independent risk factors.

## Disclosure

The data reported are propriety to the Instituto Nacional de Salud Pública, México.

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