

Incidence and prevalence of Diabetes mellitus type 2 in people receiving care for HIV in a third level health care center in Mexico City

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Palabras clave: Antirretroviral, comorbilidad, diabetes mellitus, infección por VIH, prevalencia
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Resumen

Introducción

La carga global de diabetes mellitus tipo 2 (DM2) ha ido en aumento en las últimas décadas, y en México es la principal causa de muerte desde el 2000. Avances en la expectativa de vida de personas que viven con VIH (PVCVIH) ha conducido al aumento de enfermedades crónico-metabólicas y cardiovasculares como la DM2. La información acerca de la prevalencia de DM2 entre PVCVIH es insuficiente, por lo que estimamos la incidencia y prevalencia anual de DM2 entre personas PVCVIH en México.

Material y Métodos

A través de un análisis retrospectivo de una cohorte de adultos recibiendo atención en el INCMNSZ entre 2000-2017 se estimó la incidencia y prevalencia anual de DM2 entre pacientes que recibían atención activamente en cada año del estudio.

Resultados

De un total de 3338 pacientes incluidos, 123 fueron identificados como pacientes con diabetes al final del periodo de estudio. La prevalencia anual de diabetes entre los pacientes atendidos en la clínica se incrementó de 2.4% en 2000 a 4.5% en 2017; la mediana de edad al diagnóstico de DM2 fue 42.15 años, con una mediana de 7.45 años posteriores al diagnóstico de VIH. Además, el número de cualquier comorbilidad entre los pacientes con DM2 fue mayor (4 vs 1, $p < 0.001$), de las cuales las enfermedades no-relacionadas al VIH fueron más frecuentes entre los pacientes con DM2 (3 vs 1, $p < 0.001$).

Discusión

En resumen, nuestros hallazgos revelan que entre una población de adultos infectados con VIH recibiendo atención en el INCMNSZ, la DM2 fue una comorbilidad relativamente infrecuente, aunque con un número elevado de comorbididades.

Palabras clave: *antirretroviral, comorbilidad, diabetes mellitus, infección por VIH, prevalencia*

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Abstract

Introduction.

The diabetes mellitus type 2 (T2D) burden is rising worldwide, and in Mexico it has been the leading cause of death since 2000. Improved life expectancy of people living with HIV (PLWH) have led to an increase in chronic diseases such as T2D in such population. Estimates of T2D prevalence among HIV-infected adults are lacking, thus we assessed the annual incidence and prevalence of T2D among PLWH in Mexico.

Material and Methods.

A retrospective analysis using cohort data of adults receiving care for HIV at the INCMNSZ between 2000-2017 by performing a series of annually repeated cross-sectional analysis to estimate the annual prevalence and incidence of T2D among all people actively receiving care each year, during the study period.

Results.

During the period of the study, 3,338 patients were included and 123 were identified as diabetic at the end of follow-up. The annual prevalence of T2D among people receiving care for HIV increased from 2.4% in 2000 to 4.5% in 2017; the median age of T2D diagnosis was 42.15 years after a median of 7.45 years of HIV diagnosis. Also, overall comorbidities were more common in T2D patients (4 vs 1, $p < 0.001$) when compared to non-T2D from which non-AIDS defining events were more frequent among people with diabetes (3 vs 1, $p < 0.001$).

Discussion.

Our findings revealed that among a population of adults receiving care for HIV at the INCMNSZ, T2D was a relatively infrequent comorbidity but with a high burden of comorbidities.

Key Words: antiretroviral, comorbidity, diabetes mellitus, HIV infection, prevalence

Background

Type 2 diabetes mellitus (T2D) is a prominent public health problem in Mexico. In 2016, the prevalence of T2D in the adult population was 9.4%.¹ Population growth, aging, and major changes in lifestyle have all contributed to an increased prevalence of T2D.² In Mexico since the year 2000, diabetes mellitus is the lead cause of death in women and the second most common cause in men in Mexico, just after coronary heart disease, a condition that is frequently result from T2D.³ Moreover, T2D is a progressive condition for which continuous medical care is required to minimize the risk of acute and long-term complications.⁴ Treatment often require a multiple drugs approach, and the choice between different agents depend to each patient's profile^{5,6} and yet, comorbidity usually exists and increases in old age⁷ jeopardizing treatment options, as interaction between drugs and complications from diabetes can occur.^{8,9}

Advances in treatment of HIV infection have led to decreased mortality and increased life expectancy among HIV-infected persons.^{10,11} Therefore, chronic metabolic and cardiovascular diseases such as T2D are gaining importance as causes of morbidity and mortality among people living with HIV (PLWH).¹² The co-existence of T2D has been associated to increased risk of disability,¹³ psychomotor impairment of probable vascular origin,¹⁴ chronic kidney disease,¹⁵ and may further increase the risk of tuberculosis

among PLWH.¹⁶ Thus, increasing cost of health care for PLWH associated to an increasing frequency of chronic comorbidities, including diabetes, are predictable.¹⁷

Hence, estimating the frequency of T2D among PLWHIV is important for health care services planning. While the burden of T2D among the general Mexican adult population has been previously described,¹⁸ estimates of T2D prevalence among HIV-infected adults are lacking. Thus, we used cohort data from the HIV/AIDS Clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) to assess the annual incidence and prevalence of T2D among people living with HIV in Mexico.

Methods

Study setting

The HIV/AIDS Clinic is located at the INCMNSZ, a third-level referral hospital in Mexico City administrated by the Secretaría de Salud in México. The HIV Clinic is one the oldest and largest centers for HIV care in the country with more than 2,000 active patients. Our center serves as referral site for management of complex health problems including patients with advanced HIV associated disease, neoplasias, HCV co-infection, and extensive antiretroviral resistance.

Study design

We conducted a retrospective analysis using cohort data of

all HIV, actively infected adults receiving at the INCMNSZ with at least one visit after being enrolled in the clinic, during each calendar year within the study period (2000-2017). We performed a series of annually repeated cross-sectional analysis to estimate the annual prevalence and incidence of T2D among all people actively receiving care each year during the study period.

Definitions and data collection

We defined “actively receiving care” if the patient had at least one visit during the year. Each patient contributed with data each year as long as they continued actively in care for that year. The definition of T2D was based on registered diagnosis on the clinic’s database. The diagnosis can be either self-reported, diagnosed or confirmed in our center based on international normative diagnostic criteria.⁵ Body mass index (BMI) was calculated as the ratio of weight in kilograms to the square of height in meters. We used for this analysis date of enrollment to care, HIV diagnosis and T2D diagnosis, in addition to sociodemographic and clinical information.

We retrieve data from the HIV/AIDS clinic database that prospectively collects information on all patients receiving care in our clinic as part of our collaboration with the Caribbean, Central and South America network for HIV epidemiology (CCASAnet).¹⁹ Ascertainment of any new AIDS-defining events (ADEs) and non-AIDS-defining events (NADEs) is performed by the attending physicians and fellows every medical visit, registered in standardized print formats, and manually collected by data managers. The database is subjected routinely to internal and external audits and errors correction for quality control purposes.²⁰

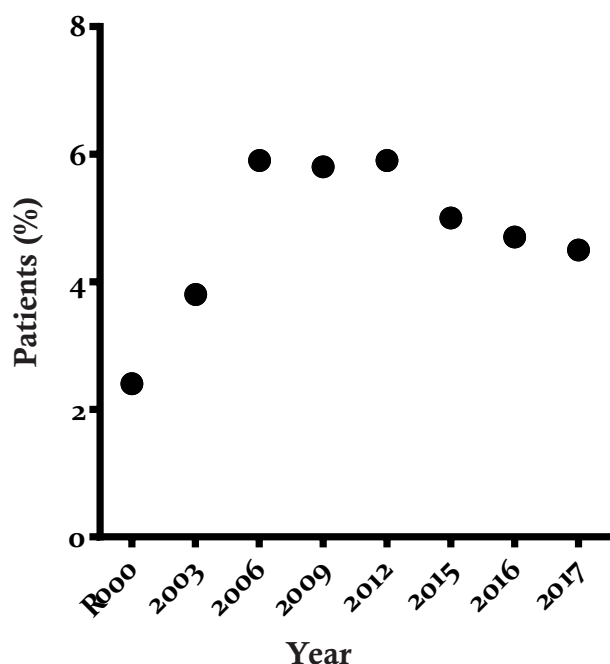


Figure 1. Annual prevalence of T2D in people actively receiving HIV care at HIV/AIDS Clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico City, from 2000-20017

To calculate the prevalence of T2D, the total number of people receiving HIV care each year was used as denominator and the total number of people receiving HIV care with T2D as numerator.

Statistical methods

We summarized data as medians (IQR) for continuous variables, and as percentages for categorical variables. We compared sociodemographic and clinical characteristics between patients diagnosed with T2D and their counterparts using the Kruskal-Wallis test for continuous variables, and chi-square test and Fisher-exact test to compare proportions of categorical variables. We calculated the percentage of patients with T2D relative to the total number of patients active in care by calendar year. We estimated unadjusted incidence dividing the annual proportion of newly diagnosed cases of T2D over patients actively receiving care per year. Analyses were performed using STATA Software (version 14).

Ethical considerations

The Scientific and the Ethics Committees of the INCMNSZ have approved the use of anonymized, demographic and clinical data collected during routine care of our patients for research purposes as part of the CCASAnet project. We comply with the principles of the Declaration of Helsinki.²¹

Results

Frequency of Diabetes mellitus among people receiving care for HIV.

There were 3338 patients actively receiving care at any given year between 2000 and 2017. Only 123 (3.95%) of them were registered as having T2D at any time while receiving care. The annual prevalence of diabetes among people receiving care for HIV increased from 2.4% in 2000 to 4.5% in 2017 (Figure 1). In 2000, there were 15 (3.3%) patients diagnosed with T2D among 454 receiving care for HIV (11 prevalent cases and 4 incident cases). In average, five patients were diagnosed with T2D each year (Table 1). In the years of 2004 and 2006, ten patients were diagnosed each with T2D, while no new cases of T2D were identified in 2013. The prevalence of T2D steadily increased since 2000 until a peak of 6.1% in 2011 was reached; in the following years a sustained decrease trend, which accentuated in 2015-2016 (5% to 4.7%), was observed until the end of follow up. Patients receiving care in our clinic increased from 454 patients in 2001 to nearly 2,000 in 2017; in average 86 additional patients became active each year. We recorded 198 deaths during follow up, from which eight were diabetic patients.

Characteristics of patients with HIV by Diabetes status

Median age at diabetes diagnosis was 42.15 years; and, by the date of their last visit had been diagnosed with T2D for 9.56 years (IQR 6-15). Most patients (n=92, 75%) were diagnosed with T2D while receiving care for HIV. In average, 7.45 (IQR 4-11) years after being diagnosed with HIV. People with Diabetes were older (44 vs 34 years, $p<0.001$), less educated (11 years vs 13 years, $p=0.013$), with higher BMI (24 vs 22, $p=0.002$), had been living longer with HIV (15.09 years vs 6.96 years, $p<0.001$), had more AIDS at any given time (47% vs 35%, $p=0.006$), and had more comorbidities (4 vs 1, $p<0.001$). Also, non-AIDS defining events were more

Tabla 1. Annual incidence and prevalence of DM2 among people actively receiving care for HIV at the HIV/AIDS Clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico City (2000-2017)

Enrollment year	Diabetic diagnosis incidence ^a	Diabetic prevalence (%) ^b	Total active
2000	4	11(2.4)	454
2001	7	16 (3.3)	490
2002	1	19 (3.4)	553
2003	4	25 (3.8)	662
2004	10	36 (4.8)	746
2005	8	47 (5.6)	836
2006	10	53 (5.9)	894
2007	5	52 (5.5)	954
2008	9	61 (5.7)	1078
2009	5	68 (5.8)	1163
2010	9	77 (6)	1267
2011	8	84 (6.1)	1366
2012	3	87 (5.9)	1462
2013	0	87 (5.4)	1597
2014	1	86 (5.1)	1665
2015	1	89 (5)	1773
2016	3	89 (4.7)	1864
2017	2	87 (4.5)	1892

a. New cases of diabetes per calendar year.

b. Out of total active patients

frequent among people with T2D (3 vs 1, $p < 0.001$). The percentage of male patients, socioeconomic status and frequency of AIDS-related events during follow-up were similar (Table 2).

Discussion

In this study to estimate the annual incidence and prevalence of T2D among people receiving care for HIV in Mexico, we observed an overall prevalence of 4% over a 15-year period. While the annual prevalence of diabetes had a tendency to increase the first six years, it remained low and stable around 5% after 2004 due to low incidence and increasing size of our clinic. Overall, people with T2D in our HIV clinic were 10 years older at enrolment, had higher BMI,

and had poorer health as reflected by the higher number of NADEs and co-morbidities, but also had been receiving care for HIV for longer than their non-diabetic counterparts. They were also comparatively younger when diagnosed with T2D than average age of diagnosis in Mexico which is 48 years², were less educated and notably, were enrolled in the clinic at more advanced stages of HIV associated disease, as reflected by the higher proportion of people diagnosed with AIDS and lower CD4 cells.

The prevalence of T2D in our clinic is notably lower than T2D in the adult general population in Mexico, which was estimated at 9.4% in the most recent national survey.¹ This finding was unexpected, considering that our clinic is a referral center and that previous reports have associated chronic systemic inflammation^{22,23} antiretroviral drug-induced mitochondrial dysfunction, and lipodystrophy with increased frequency of comorbidities²⁴. Selection bias through different mechanisms such as a relatively young population of adults receiving care in our clinic, low proportion of women in our cohort, higher attrition and mortality among those at risk of diabetes, and lower frequency of obesity, may account for this difference. The clear demographic and morphologic differences between patients with and without T2D partially support that traditional factors, are associated with increasing risk of T2D in an ageing population receiving care for HIV in our clinic.^{13,25-27}

Even so, in this cohort of PLWH the diagnosis of T2D was established at a mean younger age than that of the Mexican, diabetic, general population. Nevertheless, it took in average eight years in care for HIV to be diagnosed with T2D; which is consistent with a previous report in which median time to T2D development was seven years.²⁸ While chronic immune activation and persistent inflammation might have contributed to earlier onset of diabetes in our cohort, most likely, close monitoring of serum glucose during ART allowed an earlier diagnosis. Non-AIDS defining events were also more frequently observed among people with Diabetes, which is expected. There is extensive evidence that people with T2D, not-coinfected with HIV is prone to an increased prevalence of comorbidities, hospitalization rates and mortality. As both diseases accentuate and accelerate age-associated comorbidities due to heightened inflammation²⁹, further evidence is needed for better characterization of the aging mechanisms in the co-existence of diabetes and HIV.

Our study is subject to several limitations. First, our definition for diabetes was based on database report by physicians rather than through scheduled laboratory diagnostic criteria. Despite monitoring and quality control procedures²⁰ ascertainment errors might have lead us to underestimated the prevalence and incidence of diabetes in our cohort. Second, because of relatively small number of people with Diabetes, our analyses were less powered to identify some potentially important differences between groups. Third, for several of the comorbidities outcomes, we detected a substantial fraction of the conditions were not properly documented, limited to being categorized as AIDS-defining events or non-AIDS defining events. Because information of comorbidities was based on available

Table 2. Demographic and clinic characteristics of people receiving care for HIV at the HIV/AIDS Clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico City (2000-2017)

Characteristics ^a	Diabetic (n=123)	Non-diabetic (n=3215)	Total (n=3338)	p
Male	102 (83%)	2833 (88%)	2935 (88%)	0.056
Enrolment age	44 (33-53)	34 (28-42)	34 (28-41.5)	<0.001
Education years	11 (7.5-16)	13 (10.5-16)	13 (10.5-16)	0.013
Socioeconomic status ^b				
Low	47 (38%)	982 (33%)	1029 (33%)	
Middle	50 (41%)	1385 (47%)	1435 (46%)	0.578
High	26 (21%)	610 (20%)	636 (21%)	
BMI (kg/cm ²) at enrolment ^c	24 (21-26)	22 (20-25)	22.5 (20-25)	0.002
Years with HIV diagnosis at the end of follow-up	15.09 (9-19)	6.96 (3-13)	7.2 (3-13)	<0.001
Years with DM diagnosis at the end of follow-up	9.56 (6-15)	-	-	-
Age at diagnosis of DM	42.15 (31-52)	-	-	-
Years with HIV infection prior to DM diagnosis	7.47 (4-11)	-	-	-
Patients with DM diagnosis after HIV infection	92 (75%)	-	-	-
AIDS during follow-up	57 (47%)	1030 (35%)	1098 (36%)	0.006
No. Comorbidities	4 (3-5)	1 (0-3)	1 (0-3)	<0.001
AIDS defining events	0 (0-1)	0 (0-1)	0 (0-1)	0.116
Non-AIDS defining events	3 (3-4)	1 (0-2)	1 (0-2)	<0.001

a. Continuous variables are reported as medians (IQR).

b. Information available for 3,338 patients.

c. Information available for 2044 patients.

d. Information available for 3,100 patients.

e. Information available for 3,040 patients 19 with unknown data.

documentation of diagnoses, all data which was not made explicitly available was not possible to obtain through other sources. We did not include depression or anxiety among the comorbidities we examined, and these conditions may contribute significantly to the burden of disease and add-up to the non-AIDS defining events comorbidities. Finally, current information on tobacco smoking or tobacco cessation was not available; therefore, analysis for relation between diabetes and tobacco usage was not made.

Conclusions

Our findings revealed that among a population of HIV-infected adults receiving care at a tertiary center from México City, T2D was a relatively infrequent comorbidity but with a high burden of comorbidities. Our findings clarify the importance for health care professionals in Mexico providing care to PLWH to screen for T2D in patients > 40 years old and

>5 years of HIV infection, rather than only in those patients ≥ 45 years old and increased BMI as recommended by the American Diabetes Association and the USPTF.^{5,30,31} Also, our results suggest that as the Mexican population of PLWH continue to age, the frequency of diabetes is likely to increase. Our findings might be useful for planning for the integration of health care services for chronic, non-AIDS defining comorbidities, into HIV care services.

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