The Dual Threat of Diabetes and Tuberculosis in the Americas

Table of Contents

Abstract

Background/introduction: Diabetes and tuberculosis are two chronic diseases with high impact in populations of developing countries. The risk for tuberculosis is augmented by impaired host defense in individuals, such as those with HIV and diabetes. **Objective:** estimate the number of cases of TB associated with DM (TB/DM) in the Americas in 2008. **Methodology:** The number of cases of tuberculosis related to diabetes by age and gender were estimated by calculating the Population Attributable Fraction (PAF). Estimates of the prevalence of diabetes and the incidence of tuberculosis were extracted from the IDF Diabetes Atlas and the WHO Global TB Database respectively. The incidence of TB/DM is presented in number of cases per 100,000 by country. Breakdowns by age, gender, country income and geographic sub regions are also presented. **Results:** Overall 26 countries from the Americas were included in the analysis, accounting for some 528 million people of 25-79 years of age. The incidence of TB/DM was estimated at 31,411 (18, 495-53,352) cases (5.9 X 100,000 population). The risk varied among countries, with the highest risk observed in Haiti (59.3 per 100,000), and the lowest in Puerto Rico (0.9 per 100,000). **Conclusions/recommendations:** Diabetes Mellitus was estimated to be a substantial contributor to the burden of tuberculosis in the Americas Region in 2008. Because of the increased risk for tuberculosis, diabetes may contribute to the resurgence of tuberculosis in areas where it is currently under control and may impact negatively its control. It is recommended that tuberculosis screening is routinely conducted among those with diabetes especially those with uncontrolled diabetes.

Introduction

Diabetes Mellitus (DM) affects 55 Million people in the Americas and its prevalence is expected to increase to 83 Million by 2030[1]. The diabetes epidemic is driven by a similar increase in the prevalence of obesity (Body Mass Index, BMI≥30 Kg/m^2) which is a direct consequence of hyper-caloric diet and lack of physical activity. Diabetes increases the risk of cardiovascular diseases, terminal kidney disease, blindness and amputations. People suffering from diabetes require continuous care and may face premature mortality from its complications if not managed well.

Tuberculosis (TB) continues affecting millions of people worldwide, despite the widespread availability of effective treatment for many years. In the Americas approximately 280,000 people are affected by all forms of tuberculosis every year[2]. Most cases of tuberculosis are diagnosed in low-middle income countries and often concentrated in endemic areas with poor living conditions. The risk for tuberculosis is augmented by impaired host defense in individuals, such as those with HIV and diabetes[3],[4], [5].

In Mexico**,** the investigation of a national representative sample of 2,716 smear positive cases of TB showed that overall 22% of the total sampled cases were also persons with diagnosed diabetes[6]. Another recent study showed that the prevalence of TB among 345 persons with diabetes under care was 1.5%, and half of them were asymptomatic cases of TB [7]. In this study, those with diabetes were screened for tuberculosis with 3 sputum smear and monitored for diabetes control with one hemoglobin A1 (HbA1c) in Jalisco, Mexico. All cases of TB in this study were diagnosed among those with poorly controlled diabetes. A recent analysis of the impact of diabetes on the incidence of tuberculosis indicated that in India, diabetes accounted for 14.8% of cases of pulmonary tuberculosis and 20.2% of smear positive tuberculosis[8].

Giving the rising public health importance of the DM TB co morbidity and its potential costly impact on society, PAHO conducted an analysis to better document the number of cases of TB associated with DM (TB/DM) in the Americas in 2008.

Method

Data were extracted from the sources summarized in Table 1. Analyses were limited to adult population of 25 years of age and older, as estimates of the diabetes prevalence and the relative risks of incident tuberculosis associated with diabetes were available for this age group only.

Table 1. Sources of information used in calculations.

Data	Source	Estimates
Population 25-79 years	UN Population Estimates[9]	528,650,475
Prevalence of diabetes	Diabetes Atlas[1]	54,154,680
Incidence of cases of TB (all forms)	World Health Organization[10]	204,424
RR of DM/TB	Kim et al[4]	3.57 (3.07-5.16

In order to calculate country specific number of cases with diabetes and tuberculosis the prevalence of diabetes (%) and the incidence of tuberculosis (per 100,000) were multiplied by the population of participating countries. As age groups for the prevalence of diabetes and incidence of tuberculosis were not similar, prevalence of diabetes and incidence rates for TB were applied to single age population and then regrouped.

The WHO database only includes age and sex specific incidence for smear-positive cases of TB. Therefore age and sex specific incidence rates for all forms of tuberculosis were calculated by using the WHO estimates for smear-positive cases. First we calculated the ratio between age and sex specific and total number of smear positive cases of TB. Then we applied the resulted ratio for each age group to the total number of cases of TB to obtain an estimate of the total number of cases in each specific age and sex group. Also, estimates of diabetes prevalence, tuberculosis incidence and the relative risk of the incidence of tuberculosis associated with diabetes[4] were applied to age and sex specific estimates of the population of the Americas to calculate the Population Attributable Fraction (PAF).

Cases of tuberculosis related to diabetes by age and sex were estimated by calculating the Population Attributable Fraction (PAF) using formulas as described by Allison[11] and Flegal[12].

$PAF = P$ e (RR-1)/(1+(Pe(RR-1))) (1)

Pe – proportion of the population exposed to the factor
RR – unadjusted relative risk of tuberculosis associated with diabetes

Estimations were made for different subgroups within each country because of the documented variation of both the prevalence of diabetes and the risk for tuberculosis among different ages and sexes. These estimations were then summarized. Incidence upper and lower bounds were based on relative risk 95% confidence intervals[11].

To better analyze the incidence of TB/DM, countries were stratified in two different groups. First, countries were grouped by geographic sub regions namely North America, Mexico, Central America, English Caribbean, Spanish Caribbean, Andean Region and Southern Cone. Secondly countries were grouped by Gross National Product[13] in three subgroups: a) <$3,946 (Bolivia, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Nicaragua, Paraguay); b) $3,946-$12,195 (Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Rep, Jamaica, Mexico, Panama, Peru, Uruguay, Venezuela); and c) >$12,195(Canada, Puerto Rico, Trinidad & Tobago, United States of Americas).

Incidence of TB, incidence of DM/TB and prevalence of DM by country were standardized by the direct method using the world population as standard[14]. The prevalence of diabetes is presented in percentages (%), while the incidence of tuberculosis and tuberculosis/diabetes are presented in number of cases per 100,000 populations.

Results

Overall 26 countries from the Americas were included in the analysis, accounting for some 528 million people of 25-79 years of age. Table 2 shows the prevalence of diabetes and the incidence of TB by country.

Table 2. Age-and-sex standardized estimated prevalence of DM (%) and incidence of TB (X100,000) among those 25-79 years of age by country in 2008.

	TB			DM			TB/DM		
	CASES	%	%*	CASES	Rate	Rate*	CASES	Rate	Rate*
Argentina	8,329	36.6	37.0	1,561,691.63	6.9	6.8	998	4.4	4.4
Bolivia	8,268	189.3	197.7	269,116.04	6.2	7.1	1,053	24.1	24.9
Brazil	69,231	63.5	64.1	7,496,186.10	6.9	7.5	9,602	8.8	8.8
Canada	1,323	5.9	5.9	2,833,724.38	12.6	10.9	253	1.1	1.1
Chile	1,581	15.8	16.0	689,175.27	6.9	6.7	216	2.2	2.1
Colombia	12,126	50.5	54.2	1,338,870.44	5.6	6.2	1,312	5.5	5.8
Costa Rica	384	15.3	15.4	255,873.64	10.2	10.9	77	3.1	3.0
Cuba	583	7.9	7.8	887,841.59	12.1	11.1	116	1.6	1.5
Dominican R	5,242	105.2	102.7	598,146.71	12.0	13.1	1,215	24.4	23.2
Ecuador	6,823	100.5	100.1	436,905.03	6.4	7.0	893	13.2	12.9
El Salvador	1,530	53.3	55.9	280,847.03	9.8	10.4	291	10.1	10.6
Guatemala	6,479	120.6	129.3	449,209.21	8.4	10.0	1,188	22.1	24.1
Guyana	690	172.2	164.7	43,370.74	10.8	11.2	147	36.6	34.0
Haiti	16,097	371.9	354.1	307,945.68	7.1	8.4	2,567	59.3	57.1
Honduras	3,454	110.7	118.4	269,843.86	8.6	10.6	657	21.1	22.2
Jamaica	134	9.9	10.2	165,065.82	12.1	12.3	28	2.0	2.0
Mexico	15,980	27.4	29.0	6,653,759.57	11.4	12.6	3,422	5.9	6.0
Nicaragua	1,827	72.8	75.6	241,359.40	9.6	11.7	377	15.0	15.5
Panama	1,242	67.5	68.3	192,926.46	10.5	11.3	262	14.3	14.0
Paraguay	2,145	73.5	74.8	146,084.91	5.0	5.7	244	8.4	8.5
Peru	20,585	139.9	139.3	954,347.37	6.5	7.3	2,821	19.2	18.7
Puerto Rico	101	4.1	4.2	344,306.69	13.9	12.4	22	0.9	0.9
Trinidad & T	270	33.3	35.8	107,835.78	13.3	13.7	61	7.5	7.7
USA	12,265	6.2	6.3	26,471,633.45	13.5	12.0	2,518	1.3	1.3
Uruguay	581	29.4	31.0	145,809.18	7.4	6.8	72	3.7	3.8
Venezuela	7,153	48.4	50.4	1,012,804.88	6.9	7.7	998	6.8	6.9
TOTAL	204,424	38.7	-	54,154,680.82	10.2	-	31,411	5.9	-

* Standardized by age-and-sex by the direct method using the world population as standard

Table 3 presents the incidence of tuberculosis related to diabetes (number and rates per 100,000 population) by country.

Table 3. Age-and-sex standardized estimated incidence of diabetes/tuberculosis (X100,000) among those 25-79 years of age by country in 2008.

COUNTRY	NUMBER OF CASES	BOUND		Ratex100,000	
		LOWER	UPPER	CRUDE	STANDARDIZED*
Argentina	998	589	1,666	4.4	4.4
Bolivia	1,053	593	1,861	24.1	24.9
Brazil	9,602	5,749	16,576	8.8	8.8
Canada	253	133	424	1.1	1.1
Chile	216	128	361	2.2	2.1
Colombia	1,312	732	2,191	5.5	5.8
Costa Rica	77	47	126	3.1	3.0
Cuba	116	74	175	1.6	1.5
Dominican R	1,215	802	1,912	24.4	23.2
Ecuador	893	532	1,540	13.2	12.9
El Salvador	291	171	492	10.1	10.6
Guatemala	1,188	712	1,986	22.1	24.1
Guyana	147	99	223	36.6	34.0
Haiti	2,567	1,574	4,626	59.3	57.1
Honduras	657	390	1,111	21.1	22.2
Jamaica	28	17	43	2.0	2.0
Mexico	3,422	1,945	5,545	5.9	6.0
Nicaragua	377	230	635	15.0	15.5
Panama	262	165	421	14.3	14.0
Paraguay	244	145	428	8.4	8.5
Peru	2,821	1,680	4,834	19.2	18.7
Puerto Rico	22	13	34	0.9	0.9
Trinidad & T	61	38	92	7.5	7.7
USA	2,518	1,335	4,215	1.3	1.3
Uruguay	72	44	118	3.7	3.8
Venezuela	998	557	1,716	6.8	6.9
TOTAL	31,411	18,495	53,352	5.9	-

* Standardized by age-and-sex by the direct method using the world population as standard

Incidence of Tuberculosis

The overall incidence of tuberculosis for the Americas in 2008 was estimated in 38.7 per 100,000 population (204,424 cases), with the highest rate reported for Haiti followed by Bolivia and Guyana, all three countries with incidence of more than 172 per 100,000 (Figure1). The lowest rate was found in Puerto Rico, followed by Canada and Uruguay, all with less than 7 cases per 100.000. The estimated number of cases of TB was much higher among males than among females (Figure 2). Male to female (M:F) ratio in the risk for tuberculosis was the highest in Jamaica where four men for every one women was estimated to have TB. The lowest M:F ratio was found in Haiti where men and women had almost the same risk.

Figure 1. Estimated incidence (X 100,000) of tuberculosis by country, 2008

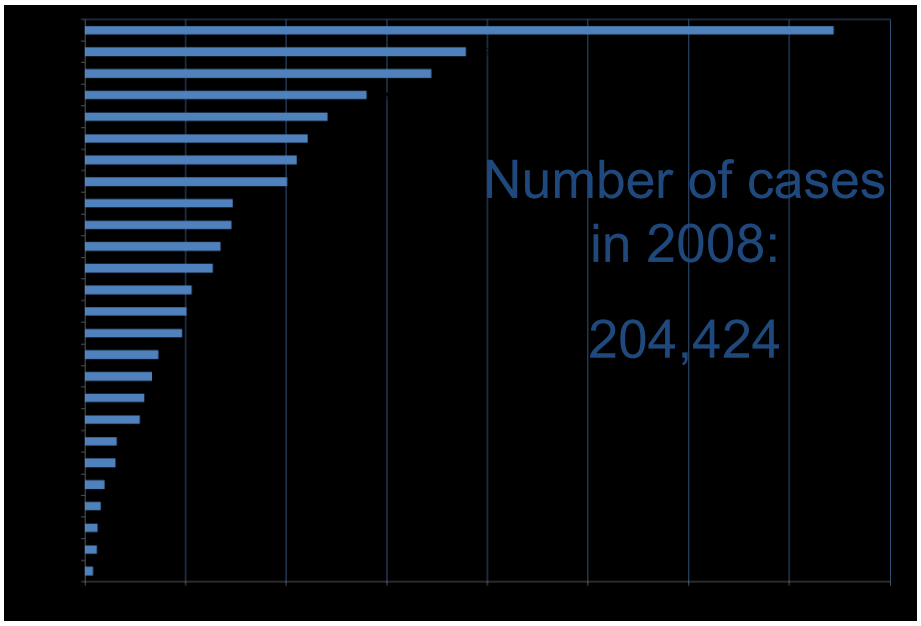
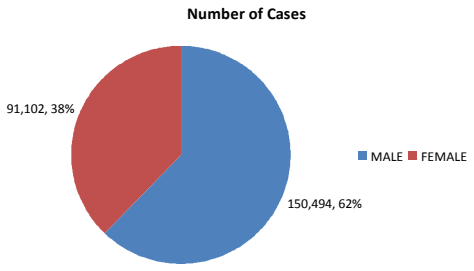


Figure 2. Cases of tuberculosis (number, %) by sex



Prevalence of Diabetes

The prevalence of diabetes was estimated in 10.3 % (54 millions people) with the highest risk by country reported in Puerto Rico followed by the United States and Trinidad and Tobago, all with more than 13% of the population 25-79 years of age. The smallest risk was estimated in Paraguay with 5%. Prevalence of diabetes increases with age in both men and women. Among men and women the prevalence of diabetes is comparable within each age group.

Incidence of Tuberculosis Associated to Diabetes

The incidence of TB/DM was estimated at 5.9 X 100,000 population (31,411 cases, with lower and upper bounds estimated at 18,495 and 53,352 respectively). The incidence varied among countries with the highest figure observed in Haiti with 59.3 per 100,000, and the lowest in Puerto Rico with 0.9 per 100,000.

The incidence of tuberculosis related to diabetes peaked among those of 35 to 44 years of age for both men and women and was much higher among men than women

Figure 3. Incidence (X 100,000) of tuberculosis related to diabetes by age and gender, 2008

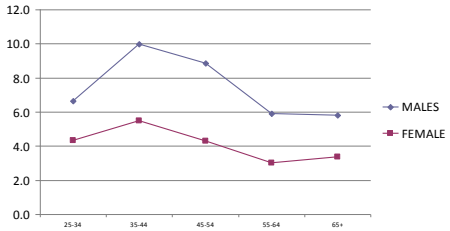
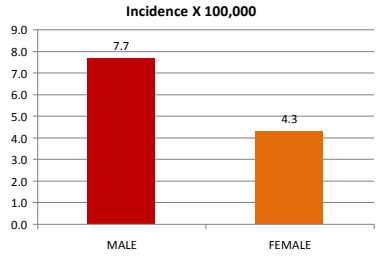


Figure 4. Incidence (X100,000) of tuberculosis and diabetes by sex, 2008



The risk developing tuberculosis related to diabetes was the highest among those countries from the English Speaking Caribbean followed by Central America. The Southern Cone and Lower-Middle income countries accounted for the biggest number of cases given their bigger population.

Figure 5. Number of cases of tuberculosis related to diabetes by Sub Region, 2008

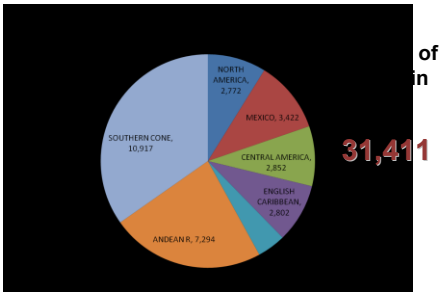


Figure 6. Incidence (X100,000) of tuberculosis and diabetes by Sub Region, 2008

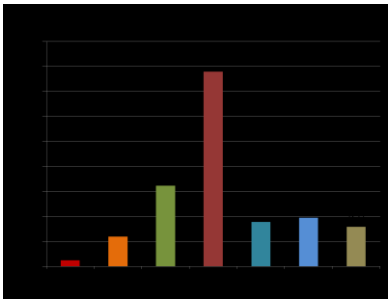
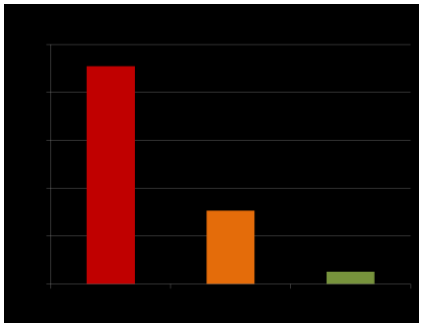


Figure 7. Incidence (X100,000) of tuberculosis and diabetes by country GNP, 2008



Limitations

The lack of complete data is a limitation of this analysis. In the first place, data sources used for the prevalence of diabetes came from estimates produced by the International Diabetes Federation and not from real prevalence studies, which are not available for most countries in the Americas. Secondly, the WHO data on the incidence of tuberculosis is not desegregated by age and sex and therefore the estimates were calculated using the distribution by age and sex of smear-positive tuberculosis. This may introduce biases that are beyond our control. Third, as the breakdown groups by age and sex of the used data (smear positive TB, prevalence of diabetes and Relative Risk for tuberculosis among those with diabetes) were not similar, we used the UN population estimates that are presented by single age. This UN population may differ slightly from the original population used to calculate each original data. Finally, the obtained incidence of tuberculosis and tuberculosis/diabetes were calculated only for the population 25-79 years of age. As our rates exclude the population under 25 years of age which is at low risk for tuberculosis, the resulting incidence rates may look slightly higher than those normally seen for the whole population.

Conclusions

Diabetes mellitus was a substantial contributor to the burden of tuberculosis in the Americas Region in 2008, accounting for an estimated 31,411 cases or 15.4% of the total number of cases of tuberculosis. Because of the increased risk for tuberculosis, diabetes may contribute to the resurgence of tuberculosis in areas where it is currently under control and may impact negatively its control. On the other hand it is unclear how many of these cases of tuberculosis are asymptomatic, remaining undiagnosed for a long time in the communities. These undiagnosed cases may contribute further to the spread of tuberculosis among susceptible individuals. The projected increase in the prevalence of diabetes that is expected to occur globally soon may interfere with the achievement of the Millennium Development Goals as it will increase enormously the risk for tuberculosis.

Recommendations

It is recommended that tuberculosis screening is routinely conducted among those with diabetes especially those with uncontrolled diabetes. Control of diabetes mellitus should be undertake as a strategy for decreasing the burden of tuberculosis

As both diabetes and tuberculosis can be asymptomatic, screening for these diseases should not be based on the presentation of classic symptoms but rather on the presence of risk factors.

Diabetes screening with fasting blood glucose or Hemoglobin A1c should be conducted among those under treatment for tuberculosis. For those with tuberculosis, the screening for diabetes should be based on the presence of major risk factors such as those 40 years of age or older, obese or overweight individuals, those with family history of diabetes and a personal history of hyper glycemia or gestational diabetes.

Proactive tuberculosis opportunistic screening is recommended for those with uncontrolled diabetes; especially those living in countries with higher risk for tuberculosis/diabetes as shown in this analysis. Although those with diabetes and respiratory symptoms are at extremely high risk for tuberculosis, the simple presence of uncontrolled diabetes should trigger an alarm strongly indicating that these patients should be screened for tuberculosis.

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