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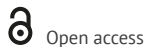
Mortality in patients with multidrug-resistant tuberculosis in a tertiary care hospital in Lima, Peru

Mortalidad en pacientes con tuberculosis multidrogoresistente en un hospital de tercer nivel de Lima, Perú

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Abstract

Introduction: In recent years, an increase in the number of multidrug-resistant (MDR) tuberculosis (MDR-TB) cases has been reported worldwide. This implies an increase in mortality rates due to the complex treatment of MDR-TB and the presence of different risk factors in these patients.

Objective: To determine the risk factors for mortality in patients with MDR-TB treated at the pulmonology service of the Hospital Nacional Dos de Mayo (Lima, Peru) between 2014 and 2018.

Materials and methods: Retrospective case-control study conducted in 305 MDR-TB patients hospitalized between 2014 and 2018 (cases: 62; controls: 243). Cases were defined as patients who died. Data on variables of interest were obtained from medical records. A bivariate and a multivariate analysis (logistic regression model) were performed by calculating odds ratios (crude and adjusted) to determine the association between the variables considered in this study and mortality.

Results: Participants' mean age was 48.2±19.4 years. In the multivariate analysis, having diabetes mellitus (aOR: 8.580, 95%CI: 1.805-40.785), having a history of TB (aOR: 4.923, 95%CI: 1.474-16.446), being an active smoker (aOR: 12.189, 95%CI: 3.047-48.759), using psychoactive drugs (aOR: 9.428, CI95%: 2.737-32.482), and being malnourished (aOR: 6.652, CI95%: 1.432-30.888) were associated with an increased risk of mortality due to MDR-TB.

Conclusions: In this study, several risk factors for mortality in MDR-TB patients were identified. Strategies for the adequate management of MDR-TB, particularly in patients with the mortality risk factors identified here, must be implemented at the Hospital Nacional Dos de Mayo, as well as other hospitals that provide healthcare services to these patients in Lima.

Resumen

Introducción. En los últimos años se ha reportado un aumento en el número de casos de tuberculosis (TB) multidrogoresistente (MDR) a nivel mundial. Esto implica un incremento en las tasas de mortalidad debido a que el tratamiento de la TB-MDR es complejo y a la presencia de diferentes factores de riesgo en estos pacientes.

Objetivo. Determinar los factores de riesgo de mortalidad en pacientes con TB-MDR atendidos en el Servicio de Neumología del Hospital Nacional Dos de Mayo (Lima, Perú) entre 2014 y 2018.

Materiales y métodos. Estudio retrospectivo de casos y controles realizado en 305 pacientes con TB-MDR hospitalizados entre 2014 y 2018 (casos: 62; controles: 243). Los casos se definieron como aquellos pacientes que fallecieron. Los datos de las variables de interés se obtuvieron de las historias clínicas. Se realizó un análisis bivariado y uno multivariado (modelo de regresión logística) mediante el cálculo de *odds ratio* (crudos y ajustados) para determinar la asociación entre las variables consideradas y la mortalidad.

Resultados. El promedio de edad fue 48.2±19.4 años. En el análisis multivariado, tener diabetes *mellitus* (ORa: 8.580, IC95%: 1.805-40.785), tener antecedente de TB (ORa: 4.923, IC95%: 1.474-16.446), la presencia de tabaquismo (ORa: 12.189, IC95%: 3.047-48.759), la presencia de consumo activo de sustancias psicoactivas (ORa: 9.428, IC95%: 2.737-32.482) y estar desnutrido (ORa: 6.652, IC95%: 1.432-30.888) se asociaron con un mayor riesgo de mortalidad por TB-MDR.

Conclusiones. En el presente estudio se identificaron varios factores de riesgo de mortalidad en pacientes con TB-MDR. En el Hospital Nacional Dos de Mayo, así como en otros hospitales de Lima que atiendan estos pacientes, se deben implementar estrategias para el manejo adecuado de la TB-MDR, en particular en pacientes con los factores de riesgo de mortalidad aquí identificados.

Introduction

Tuberculosis (TB) is one of the leading causes of death worldwide despite being a preventable and curable infectious disease. According to the Global Tuberculosis Report 2020,¹ there has been a significant increase in multidrug-resistant (MDR) TB cases in recent years,¹ which is defined as TB resistant to both rifampicin and isoniazid, two first-line anti-TB drugs. Moreover, as of 2017, 15% of people with MDR-TB died and only 57% successfully completed treatment (i.e., cured or completed treatment).¹

Several factors associated with an increased risk of mortality in TB cases have been described, some of which are patient-specific, such as male sex, ages >60 years old, history of diabetes mellitus (DM), HIV co-infection, and history of TB, especially in cases with incomplete prior treatment or with extremely resistant TB who received treatment for MDR-TB.² Associated socio-environmental behaviors such as smoking, alcoholism and psychoactive substance use have also been reported.²⁻⁴ In this sense, studies are needed to determine the association of demographic, socio-environmental and clinical variables with mortality in people with MDR-TB in order to establish measures aimed at reducing the risk of mortality in these patients.

Considering the foregoing, the objective of the present study was to determine the risk factors for mortality in MDR-TB patients treated at the pulmonology service of the Hospital Nacional Dos de Mayo (Lima, Peru) between 2014 and 2018.

Materials and methods

Study type

Retrospective case-control study.

Population and sample

The study population included all patients older than 15 years with MDR-TB diagnosis admitted between 2014 and 2018 to the Hospital Nacional Dos de Mayo (N=305). To calculate sample size, an odds ratio (OR) of 2 was considered, with an exposure of 50% for controls and a confidence level of 95%. Non-probabilistic sampling was performed. Taking into account the above, a minimum sample size of 45 cases and 90 controls was obtained.

In this study, cases were defined as patients who died from MDR-TB (death from tuberculosis was defined as mortality from any cause before completion of anti-tuberculosis treatment according to the World Health Organization), and controls were defined as those who did not die.

In order to recruit participants, the following exclusion criteria were considered: patients whose reason for hospitalization was not related to TB, patients with incomplete data in their medical records on the variables of interest, and patients who reported an adverse drug reaction. Since none of the 305 patients considered in the study population met these exclusion criteria, it was decided to include all of them in the final sample (cases: 62; controls: 243).

Procedures and variables

The patients' medical records were reviewed in order to collect data on the variables of interest (described in the following paragraph) by means of a data collection form validated by experts from the Hospital Nacional Dos de Mayo. These data were entered and arranged in a spreadsheet created in Microsoft Excel for subsequent analysis.

The following variables of interest were considered: categorical variables: MDR-TB mortality, sex, age group (15-29 years, 30-49 years, ≥ 50 years), educational level (primary, secondary, and higher education [university and non-university]), nutritional status (malnutrition, normal/overweight), previous contact with people with TB, history of TB (prior TB infection), presence of extrapulmonary TB, type of TB (central nervous system [CNS], pleural, intestinal, multisystemic, and others), history of DM, HIV coinfection, active smoking, alcohol consumption, and use of psychoactive substances; quantitative variables: age, body mass index, height, and weight.

Statistical analysis

Data are described using absolute and relative frequencies for qualitative variables and means and standard deviations for quantitative variables. A bivariate analysis was performed by calculating the ORs, with their respective 95% confidence intervals (95%CI) to establish the association between the variables included and the risk of mortality; a significance level of $p < 0.05$ was considered. It should be noted that, for this analysis, age was categorized into < 50 and ≥ 50 years. The statistical analysis was conducted in the SPSS software (version 20).

Finally, a multivariate analysis was performed using a logistic regression model in which all variables with statistical significance in the bivariate analysis were included to identify the factors associated with an increased risk of mortality in these patients.

Ethical considerations

The study followed the ethical principles for biomedical research involving human subjects established in the Declaration of Helsinki.⁵ In addition, it was reviewed and approved by the Ethics Committee of Universidad Privada San Juan Bautista in accordance with minutes No. 2898 of February 25, 2019. The anonymity of the patients was guaranteed throughout the research process and, since the study was based on a medical record review, it was not necessary to sign an informed consent form.

Results

Of the 305 patients, 75.41% were male and 59.67% had completed secondary education. The mean age was 43.76 years for cases and 49.37 years for controls. In addition, 39.67% had a history of TB and 14.43% and 36.72% had DM and HIV, respectively. The most frequent harmful habit was alcohol consumption (42.95%), followed by smoking (28.19%), and psychoactive substance use (22.95%). Regarding the type of TB, 42.29% ($n=129$) had extrapulmonary TB, with CNS-TB being the most frequent (53.48%). Finally, severe malnutrition was found in 43.85% of the cases and 4.97% of the controls (Table 1).

Table 1. Clinical epidemiological variables of patients with multidrug-resistant tuberculosis treated between 2014 and 2018 at the Hospital Nacional Dos De Mayo in Lima, Peru.

Risk factors			Total (n=305)	Cases (n=62)	Controls (n=243)
			n (%)	n (%)	n (%)
Age group	15-29 years old		62 (20.33%)	17 (27.42%)	45 (18.52%)
	30-49 years old		104 (34.10%)	23 (37.10%)	81 (33.33%)
	≥50 years old		139 (45.57%)	22 (35.48%)	117 (48.15%)
Age (mean ± SD)			48.23±19.39%	43.76±18.55	49.37±19.47
Sex	Male		230 (75.41%)	48 (77.42%)	182 (74.90%)
	Female		75 (24.59%)	14 (22.58%)	61 (25.10%)
Educational level	Primary		54 (17.71%)	16 (25.81%)	38 (15.64%)
	Secondary		182 (59.67%)	43 (69.35%)	139 (57.20%)
	Higher		69 (22.62%)	3 (4.84%)	66 (27.16%)
Contact with people with TB	Yes		150 (49.18%)	54 (87.1%)	96 (39.51%)
	No		155 (50.82%)	8 (12.9%)	147 (60.49%)
History of TB	Yes		121 (39.67%)	52 (83.87%)	69 (28.40%)
	No		184 (60.33%)	10 (16.13%)	174 (71.60%)
Extrapulmonary TB	Yes		129 (42.30%)	24 (38.71%)	105 (43.21%)
	No		176 (57.70%)	38 (61.29%)	138 (56.79%)
Type of extrapulmonary TB*	Central nervous system		69 (54.48%)	15 (62.5%)	54 (51.42%)
	Pleural		33 (25.57%)	3 (12.5%)	30 (28.57%)
	Intestinal		13 (10.07%)	1 (4.16%)	12 (11.42%)
	Multisystemic		3 (2.31%)	2 (8.33%)	1 (0.95%)
	Others		11 (8.52%)	3 (12.5%)	8.2 (7.62%)
Diabetes mellitus	Yes		44 (14.43%)	22 (35.48%)	22 (9.05%)
	No		261 (87.57%)	40 (64.52%)	221 (90.95%)
HIV co-infection	Yes		112 (36.72%)	36 (58.06%)	76 (31.28%)
	No		193 (63.28%)	26 (41.94%)	167 (68.72%)
Active smoking	Yes		86 (28.20%)	55 (88.71%)	31 (12.76%)
	No		219 (71.80%)	7 (11.29%)	212 (87.24%)
Alcohol use	Yes		131 (42.95%)	57 (91.94%)	74 (30.45%)
	No		174 (57.05%)	5 (8.06%)	169 (69.55%)
Active use of psychoactive substances	Yes		70 (22.95%)	49 (79.03%)	21 (8.64%)
	No		235 (77.05%)	13 (20.97%)	222 (91.36%)
Weight (mean ± SD)			51.16±9.49	44.57±6.65	52.84±9.39
Height (mean ± SD)			1.66±0.61	1.66±0.55	1.65±0.62
Body mass index (mean ± SD)			18.61±2.86	16.07±2.22	19.26±2.65
Nutritional status	Normal/overweight		125 (40.98%)	4 (6.45%)	121 (49.79%)
	Malnutrition	Mild	106 (34.75%)	17 (27.42%)	89 (36.63%)
		Moderate	35 (11.48%)	14 (22.58%)	21 (8.64%)
		Severe	39 (12.79%)	27 (43.55%)	12 (4.94%)

SD: standard deviation; TB: tuberculosis; HIV: human immunodeficiency virus.

* The percentages of this variable are provided for the sample with extrapulmonary TB (n=129).

In the bivariate analysis, a significant association was observed between MDR-TB mortality and the following variables: being 50 years of age or older (OR=1.88, 95%CI: 1.047-3.400; $p=0.033$), completed primary education (OR=7.33, 95%CI: 2.222-24.201; $p=0.001$), completed secondary education (OR=1.87, 95%CI: 1.110-15.357; $p=0.001$), contact with a person with TB (OR=10.33, 95%CI: 4.711-22.679; $p=0.001$), history of TB (OR=13.11, 95%CI: 6.307-27.264; $p=0.001$), history of DM (OR=5.52, 95%CI: 2.799-10.908; $p=0.001$), history of HIV (OR=3.04, 95%CI: 1.716-5.395; $p=0.001$), active smoking (OR=53.73, 95%CI: 22.463-128.533; $p=0.001$), alcohol use (OR=26.03, 95%CI: 10.028-67.597; $p=0.001$), psychoactive substance use (OR=39.84, 95%CI: 18.677-85.007; $p=0.001$), and malnutrition (OR=14.48, 95%CI: 5.063-40.848; $p=0.001$) (Table 2).

Table 2. Bivariate analysis to establish the association between the variables considered and mortality in patients with multidrug-resistant tuberculosis treated between 2014 and 2018 at the Hospital Nacional Dos De Mayo in Lima, Peru.

Risk factors		OR	95CI%	p-value
Age (years)	≥50	1.88	1.047-3.400	0.033
	<50	1	-	
Sex	Male	1.14	0.592-2.227	0.483
	Female	1	-	
Educational level	Primary	7.33	2.222-24.201	0.001
	Secondary	1.87	1.110-15.357	
	Higher	1	-	
Contact with people with TB	Yes	10.33	4.711-22.679	0.001
	No	1	-	
History of TB	Yes	13.11	6.307-27.264	0.001
	No	1	-	
Extrapulmonary TB	Yes	1.20	0.681-2.132	0.522
	No	1	-	
Diabetes mellitus	Yes	5.52	2.799-10.908	0.001
	No	1	-	
HIV co-infection	Yes	3.04	1.716-5.395	0.001
	No	1	-	
Active smoking	Yes	53.73	22.463-128.533	0.001
	No	1	-	
Active use of psychoactive substances	Yes	39.84	18.677-85.007	0.001
	No	1	-	
Alcohol use	Yes	26.03	10.028-67.597	0.001
	No	1	-	
Nutritional status	Malnutrition	14.48	5.063-40.848	0.001
	Normal/overweight	1	-	

OR: Odds ratio; CI: confidence interval; TB: tuberculosis; HIV: human immunodeficiency virus.

In the multivariate analysis, a significant association between mortality and the following variables was observed: history of TB (OR=4.923, 95%CI: 1.474-16.446; $p=0.010$), history of DM (OR=8.580, 95%CI: 1.805-40.785; $p=0.007$), active smoking (OR=12.189, 95%CI: 3.047-48.759; $p=0.001$), psychoactive substance use (OR=9.428, 95%CI: 2.737-32.482; $p=0.001$), and malnutrition (OR=6.652, 95%CI: 1.432-30.888; $p=0.016$) (Table 3).

Table 3. Multivariate analysis: factors associated with mortality in patients with multidrug-resistant tuberculosis treated between 2014 and 2018 at the Hospital Nacional Dos De Mayo in Lima, Peru.

Deaths from TB	aOR	95CI%	p-value
Age >50 years old	0.391	0.113-1.353	0.138
Contact with people with TB	2.880	0.748-11.099	0.124
History of TB	4.923	1.474-16.446	0.010
Diabetes mellitus	8.580	1.805-40.785	0.007
HIV co-infection	0.937	0.289-3.037	0.914
Active smoking	12.189	3.047-48.759	0.001
Alcohol use	3.481	0.629-19.259	0.153
Active use of psychoactive substances	9.428	2.737-32.482	0.001
Malnutrition	6.652	1.432-30.888	0.016

aOR: adjusted odds ratio; CI: confidence interval; TB: tuberculosis; HIV: human immunodeficiency virus.

Discussion

In the present study, the demographic characteristics 'male sex' (bivariate analysis) and 'older age' (multivariate analysis) were not associated with mortality in MDR-TB patients. This finding differs from what has been reported by Alemu *et al.*,⁶ who found, in a meta-analysis that included 49 studies, that being a male (hazard ratio [HR]=1.25, 95%CI: 1.08-1.41, I^2 : 30.5%) and being over 60 years of age (HR=2.13, 95%CI: 1.64-2.62, I^2 : 59.0%; relative risk [RR]=1.40, 95%CI: 1.26-1.53, I^2 : 48.4%) are predictors of mortality in these patients. According to these authors, the presence of a higher mortality risk in the elderly may be due to the fact that this population is more likely to have chronic diseases and comorbidities. However, in the multivariate analysis of our study, being older than 50 years was not associated with mortality, which may be related to the fact that most studies that report age as a risk factor for mortality in these patients do so with an age cutoff point greater than 60 years.^{7,8}

Concerning educational level, in the bivariate analysis we found that having completed basic education, either primary or secondary, was associated with a higher risk of mortality compared to having higher education (OR=7.33 and OR=1.87; $p=0.001$). This is similar to what has been reported by several studies in which MDR-TB patients with a lower educational level have a higher probability of mortality than those with higher education. For example, Kizito *et al.*,⁸ in a study conducted with data from 198 patients who initiated MDR-TB treatment in Uganda between January 1 and December 31, 2016, reported that having no education degree was a risk factor for mortality (aOR=3.61, 95%CI: 1.1-10.4; $p=0.03$) compared to having completed primary, secondary and higher levels of education, and Chung *et al.*,⁹ who stated in a study conducted in Lima with data from 1 232 MDR-TB patients that having ≤ 6 years of education was associated with increased risk of mortality (HR=3.06, 95%CI: 1.43-6.55) compared to having ≥ 11 years of education.

On the other hand, in the multivariate analysis, we found that having DM was a risk factor for mortality (aOR=8.580, 95%CI: 1.805-40.785; $p=0.007$). In this regard, multiple studies have described DM as a risk factor for death in TB patients (MDR or not) during antituberculosis treatment.⁹⁻¹¹ This can be explained by the reduction of cellular immunity in patients with DM, since this favors the progression of TB, especially in patients with poor glycemic control. It should be kept in mind that the cause of death in these patients is not necessarily TB but rather complications of DM, such as cardiovascular disease.¹²

Furthermore, in the bivariate analysis, we found that HIV coinfection was a risk factor for mortality (OR=3.04, 95%CI: 1.716-5.395; $p=0.001$), although this association was not sustained in the multivariate analysis (ORa=0.937, 95%CI: 0.289-3.037; $p=0.914$), perhaps due to the failure to evaluate the antiretroviral treatment (ART) intervention. In this regard, the literature has described that HIV infection causes an increase in mortality among people with MDR-TB, being higher when the CD4 count is <200 cells/mL. In addition, it has been reported that deaths in TB patients can be attributed to HIV coinfection in up to 20% of cases.^{7-9,13} In view of the above, early initiation of ART is paramount, as immunosuppression causes rapid progression of TB and an increase in opportunistic infections, resulting in increased mortality.¹⁴

Other risk factors for mortality found in this study were active smoking and psychoactive substance use. In this regard, Reed *et al.*,³ in a study of 637 TB patients treated at the Masan National Tuberculosis Hospital (Korea), found that active smoking increased the risk of mortality, both for all causes of death and TB-related death, and that the combination of diabetes and smoking significantly increased the risk of death from all causes (HR=4.25, 95%CI: 1.06-17.08) and TB-related death (HR=5.78, 95%CI: 1.09-30.56) compared to non-smokers and non-diabetics.

In the multivariate analysis, we identified a significant association between the presence of malnutrition and an increased risk of mortality in MDR-TB patients (aOR=6.652, 95%CI: 1.432-30.888; $p=0.016$). Similarly, Alemu *et al.*⁶ also found that malnutrition was a predictor of mortality (HR=1.62, 95%CI: 1.28-1.97, I²: 87.2%; RR=3.13, 95%CI: 2.17-4.09, I²: 0.0%).

As for the limitations of the present study, we find that its main weakness is that no association was observed between mortality and variables with an OR <2 and that no information on ART or CD4 count of patients with HIV coinfection was reported, since this information is managed by the HIV program. Therefore, we suggest conducting more studies to identify other risk factors for mortality in MDR-TB patients. On the contrary, the main strength is that, because of its case-control design, the study identified different characteristics that pose a higher risk of mortality in Peruvian MDR-TB patients.

Conclusions

In the present study, the following risk factors for mortality in MDR-TB patients were identified: history of TB, history of DM, active smoking, psychoactive substance use, and malnutrition. In light of the above, the Hospital Nacional Dos de Mayo, as well as other hospitals in Lima and Latin America that serve this population, should implement strategies for the adequate management of MDR-TB, particularly in patients suffering from the mortality risk factors identified here. Likewise, emphasis should be placed on the early detection of TB in patients with DM.

Conflicts of interest

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References

1. World Health Organization (WHO). Global Tuberculosis Report 2020 Geneva: WHO; 2020.
2. Nicholson TJ, Hoddinott G, Seddon JA, Claassens MM, van der Zalm MM, Lopez E, *et al.* A systematic review of risk factors for mortality among tuberculosis patients in South Africa. *Syst Rev.* 2023;12(1):23. <https://doi.org/mq62>.
3. Reed GW, Choi H, Lee SY, Lee M, Kim Y, Park H, *et al.* Impact of diabetes and smoking on mortality in tuberculosis. *PLoS One.* 2013;8(2):e58044. <https://doi.org/gmvfwj>.
4. Gayoso R, Dalcolmo M, Braga JU, Barreira D. Predictors of mortality in multidrug-resistant tuberculosis patients from Brazilian reference centers, 2005 to 2012. *Braz J Infect Dis.* 2018;22(4):305-10. <https://doi.org/mrgw>.
5. World Medical Association (WMA). WMA Declaration of Helsinki - Ethical principles for medical research involving human subjects. Fortaleza: 64th WMA General Assembly; 2013.
6. Alemu A, Bitew ZW, Worku T, Gamtesa DF, Alebel A. Predictors of mortality in patients with drug-resistant tuberculosis: A systematic review and meta-analysis. *PLoS One.* 2021;16(6):e0253848. <https://doi.org/gnn7pp>.
7. Chingonzoh R, Manesen MR, Madlavu MJ, Sopeseka N, Nokwe M, Emwerem M, *et al.* Risk factors for mortality among adults registered on the routine drug resistant tuberculosis reporting database in the Eastern Cape Province, South Africa, 2011 to 2013. *PLoS One.* 2018;13(8):e0202469. <https://doi.org/gd4hk4>.
8. Kizito E, Musaazi J, Mutesasira K, Twinomugisha F, Namwanje H, Kiyemba T, *et al.* Risk factors for mortality among patients diagnosed with multi-drug resistant tuberculosis in Uganda- a case-control study. *BMC Infect Dis.* 2021;21(1):292. <https://doi.org/mrgx>.
9. Chung-Delgado K, Guillen-Bravo S, Revilla-Montag A, Bernabe-Ortiz A. Mortality among MDR-TB Cases: Comparison with Drug-Susceptible Tuberculosis and Associated Factors. *PLoS One.* 2015;10(3):e0119332. <https://doi.org/f7b7v6>.
10. Nguyen CH, Pascopella L, Barry PM. Association between diabetes mellitus and mortality among patients with tuberculosis in California, 2010-2014. *Int J Tuberc Lung Dis.* 2018;22(11):1269-76. <https://doi.org/gfhndt>.
11. Liu Y, Zheng Y, Chen J, Shi Y, Shan LY, Wang S, *et al.* Tuberculosis-associated mortality and its risk factors in a district of Shanghai, China: a retrospective cohort study. *Int J Tuberc Lung Dis.* 2018;22(6):655-60. <https://doi.org/gds9hp>.
12. Cadena J, Rathinavelu S, Lopez-Alvarenga JC, Restrepo BI. The re-emerging association between tuberculosis and diabetes: Lessons from past centuries. *Tuberculosis (Edinb).* 2019;116S:S89-97. <https://doi.org/mrgz>.
13. Bernabé-Ortiz A. Factores asociados a supervivencia en pacientes con tuberculosis en Lima, Perú. *Rev Chil Infectol.* 2008;25(2):104-7. <https://doi.org/btkr9x>.
14. De León N, Gordillo R, Chocó A, Mejía-Villatoro C. Morbi-mortalidad en pacientes con infección por *Mycobacterium tuberculosis* comprobada, y co-infección VIH-Tuberculosis en Hospital Roosevelt en Guatemala. *Avances en Enfermedades Infecciosas Guatemala.* 2016;20(Suppl 1):31-8.