Factors associated with multi-drug-resistant tuberculosis in Dakar, Senegal, 2010-2016

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Abstract

According to the World Health Organization, multidrug-resistant tuberculosis (MDR-TB) represents a major obstacle towards successful TB treatment and control. In Dakar, MDR-TB management began in 2010 with the strengthening of diagnostic resources. The objective of this study was to identify the factors associated with multidrug-resistant tuberculosis in Dakar between 2010 and 2016. We conducted a case-control study from January 10 to February 28, 2017 in tuberculosis centers in Dakar. of 169 cases and 507 controls. We used logistic regression with Epi-info version 7.2.1. to estimate the odds ratios of association. Factors significantly associated with MDR-TB were: residing in a peri-urban area (ORa=1.8; 95% CI (1.5-4.9); p=0.024), presence of MDR-TB in the entourage of patient (ORa=7.0; 95% CI (6.1-9.5); p=0.002), previous treatment failure (ORa=29.5; 95% CI (27.3-30.1); p=0.000), treatment not directly observed by a health care provider (ORa=4.3; 95% CI (4.1-7,2); p=0.000) and irregularity of treatment (ORa=1.7; 95% CI (0.5-5.4); p=0.037). Focusing interventions on population at-risk will prevent MDR-TB.

Introduction

The emergence of drug-resistant strains is undermining efforts to control tuberculosis (TB) and is a public health problem. Worldwide, according to WHO, the number of reported cases of multidrug-resistant tuberculosis (MDR-TB) in the countries that are highly affected by this form of tuberculosis has reached a worrisome proportion.[1] Approximately 190,000 deaths have been recorded, representing a case-fatality rate of 40%. In Africa, the proportion of reported MDR-TB cases is relatively low (2.2%). Given the lack of laboratories, it is likely that current figures underestimate the true burden of disease.[2] Being male,[3,4] age,[5,6] previous treatment failure or an History of previous TB treatment,[6–9] residing in a peri-urban area, history of multidrug-resistant tuberculosis in the entourage of patient are found to be factors associated with MDR-TB. The association between diabetes and MDR-TB is variously appreciated.[10-12]

In Senegal, the number of patients identified with multidrug-resistant tuberculosis has steadily increased from 36 cases in 2010 to 77 cases in 2015.In 2014, the proportion of MDR-TB was 0.5% in new cases of TB and 17.9% in previously treated cases (National Tuberculosis Control Program). In Dakar, the control of multidrug-resistant tuberculosis cases began in 2010 with the strengthening of diagnostic facilities. but the factors associated with MDR-TB are not yet known. The knowledge of these factors is crucial to guide the actors of TB care and TB prevention actions to overcome this scourge. The objective of this study was to identify the factors associated with MDR-TB among tuberculosis patients in Dakar between 2010 and 2016.

Materials and Methods

Type of study

Case-control analytical study.

Study population

The study population consisted of confirmed tuberculosis patients. A case was defined as any tuberculosis patient with a test confirming infection with Mycobacterium tuberculosis, resistant to rifampicin alone or in combination with isoniazid, registered in Dakar between January 1, 2010 and December 31, 2016. A control was defined as any patient who developed confirmed tuberculosis, registered in Dakar and reported cured at first-line treatment between January 1, 2010 and December 31, 2016.

Sampling

We took 1 case for 3 unmatched controls and used the parameters of the Fleiss formula. Therefore, we got 676 for the size of our sample, including 169 cases and 507 controls. A random sampling was performed using the patient list.

Data collection

We conducted a literature review using information sources from registry and patient records and collected socio-demographic, clinical and therapeutic characteristics on a data collection sheet.

Statistical analyses

Proportions, central tendency and dispersion measurements, odds ratios were calculated.

In the univariate analysis, we calculated the Odds ratio (OR) measuring the link between each factor with MDR-TB; all variables with p≤0.20 were included in a multivariate logistic regression. Analyses were performed with Statistical Analysis Software Epi-info version 7.2.1. For the interpretation of association, the threshold of significance retained was 5%.

Results

Socio-demographic characteristics of patients of the study

The average age was 31.2 ± 10.4 for

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cases and 33.6 ± 12.9 for controls. Ages ranged from 8.0 to 72.0 years for cases and 7.0 to 81.0 years for controls. Weight loss was noted in cases and weight gain in controls. (Table 1).

The proportion of patients with previous treatment (number of previous treatment episode greater than or equal to 1) was 47.9% in cases and 6.5% in controls. The average time to first treatment was 5.4 days for cases and 2.4 days for controls.

Univariate analysis

The socio-demographic characteristics associated with MDR-TB were 15-59 years of age and suburban residence (Table 2). The clinical characteristics associated with MDR-TB were: co-morbidity (diabetes), alcohol consumption and having MDR-TB in entourage of patient (Table 3). Therapeutic characteristics associated with MDR-TB were: previous treatment failure, treatment not directly observed (by a health worker) and irregularity of treatment (Table 4).

Multivariate analysis

After adjustment for all independent variables in the study (Table 5), the factors that remained significantly associated with MDR-TB were suburban residence (ORa=1.8; 95% CI (1.5-4.9); p=0.024), having MDR-TB in entourage of patient (ORa=7.0; 95% CI (6.1-9.5); p=0.002), previous failure (ORa=29.5; 95% CI (27.3-30.1); p=0.000), treatment not directly observed (by a health provider) (ORa=4.3; 95% CI (4.1-7,2); p=0.000), irregularity of treatment (ORa=1.7; 95% CI (0.5-5.4); p=0.037).

Discussion

In our study, the significant factors associated with MDR-TB were residing in a peri-urban area, history of multidrug-resistant tuberculosis in the entourage of patient, previous treatment failure, treatment not directly observed (by a provider) and irregularity of treatment.

Socio-demographic characteristics

Our study was not able to demonstrate an association between age and MDR-TB. A survey conducted in the Congo reported that this age group was less exposed to multidrug-resistant tuberculosis.[10] However, a 2013 study conducted in France showed that these patients were more exposed to MDR-TB than in our study.[13] This difference in results could be explained by the fact that in France, multidrug-resistant tuberculosis prevails in foreigners, who are most often young immigrants in quest of

Table 1. Description of MDR-TB cases and controls, Dakar, 2010-2016.

Characteristics		Case n (%)	Control n (%)
Age (year)	0-4	0 (0,0)	0 (0,0)
	5-14	18 (10,7)	50 (9,9)
	15-59	149 (88,2)	408 (80,5)
	≥ 60	2 (1,2)	49 (9,6)
Sex	Female	55 (32,5)	128 (25,2)
	Male	114 (67,5)	379 (74,8)
Profession	Student	34 (20,1)	79 (15,6)
	self-employed	94 (55,6)	308 (60,8)
	Employee (State)	5 (3,0)	21 (4,1)
	Retirement	1 (0,6)	19 (3,7)
	Other	5 (3,0)	4 (0,8)
	No occupation	30 (17,7)	76 (15,0)
Average weight in Kg (+/- standard deviation)	At diagnosis (W0)	54,4±11,4	51,9±10,6
	At the 1st Control (W1)	53,7±11,0	54,7±11,1
	At the 2nd Control (W2)	52,8±11,1	57,5±11,6
Weight variation (Kg)	W1-W0	-0,7	2,8
	W2-W1	-0,9	2,8
	W2-W0	-1,6	5,4
Number of previous treatment episode	0	88 (52,1)	474 (93,5)
	1	66 (39,0)	33 (6,5)
	2	12 (7,1)	0 (0,0)
	3	3 (1,8)	0 (0,0)
Average time to first treatment (+/- standard deviation)		5,4±10,3	2,4±4,9

W0: Weight at diagnostic, W1: 1st weight control at 2-3 months, W2: 2nd weight control at 6-8 months.

Table 2. Sociodemographic characteristics associated with MDR-TB cases Dakar, 2010-2016 in univariate analysis.

Socio-demographic characteristics		Cases n (%)	Controls n (%)	OR 95% CI	p
Age (year)	Less than 15 or more than 59	20 (11.8)	99 (19.5)	1	
	15-59	149 (88.2)	408 (80.5)	1.8 (1.1-3.0)	0,023
Sex	Male	114 (67.5)	379 (74.8)	1	0,064
	Female	55 (32.5)	128 (25.2)	1.4 (0.9-2.1)	0.064
Profession	Employees	6 (3,5)	21 (4.1)	1	0,733
	Unemployed	163 (96.5)	486 (95.9)	1.2 (0.5-2.9)	0.733
Area of residence	Other	126 (74.6)	419 (82.6)	1	0,021
	Peri-urban	43 (25.4)	88 (17.4)	1.6 (1.1-2.5)	0.021

Table 3. Clinical characteristics associated with MDR-TB cases Dakar, 2010-2016 in univariate analysis.

Clinical characteristics		Cases n (%)	Controls n (%)	OR 95% CI	p
HIV Infection	No	165 (97.6)	487 (96.1)	1	
	Yes	4 (2.4)	20 (3.9)	0.6 (0.2-1.7)	0.337
Diabetes	No	163 (96.4)	502 (99,0)	1	
	Yes	6 (3.6)	5 (1.0)	3.7 (1.1-12.3)	0.026
Alcohol	No	165 (97.6)	505 (99.6)	1	
	Yes	4 (2.4)	2 (0.4)	6.1 (1.1-33.7)	0.018
Tobacco	No	160 (94.7)	488 (96.2)	1	
	Yes	9 (5.3)	19 (3.8)	1.4 (0.6-3.2)	0.373
History of MDR-TBis in the entourage of patient	No	145 (85.8)	505 (99.6)	1	
	Yes	24 (14.2)	2 (0.4)	41.8 (9.8-178.9)	0.000

employment and unfavorable living conditions (precariousness, promiscuity, imprisonment ...) and therefore exposed to the disease. We found in our survey that residing in a peri-urban area was associated with multidrug resistance. The peri-urban area is comprised mainly of vulnerable population living in difficult socio-economic conditions. This peripheral zone of Dakar is mainly characterized by poorly controlled urbanization, difficult access areas, lack of basic social infrastructure, low household income, and high human concentration in households. André MK[10] showed that "people living in peri-urban households were exposed to multidrug resistance".

Clinical characteristics

Our study showed that diabetes was not significantly associated with MDR-TB. In this regard, the association between diabetes and MDR-TB is variously appreciated by the authors.[10-12] Patients having multidrug-resistant TB in their entourage were more exposed to MDR-TB. Other authors found a history of multidrug-resistant tuberculosis in the family of cases.[10] The presence of MDR-TB cases in the family is a significant determinant in the onset of the disease. Patients in close contact with MDR-TB who have tuberculosis may be suspected of multidrug resistance. Exposure to multidrug resistance is so high in these patients that it would be acceptable, according to some authors,[7,14-16] to implement a treatment similar to that of the index case while waiting for the results of the anti-tuberculosis drug susceptibility test, even if changes in treatment are required later following the test result.

Therapeutic characteristics

According to WHO, the classification of patients according to therapeutic backgrounds, makes it possible to note in our study that there was an association between multiresistance and some groups of patients (previous treatment failure). According to the meta-analysis of Faustini *et al.*, which represents a systematic review of 29 publications, failure of prior anti-tuberculous therapy increased exposure to a multidrug-resistant strain by up to 10 times.[7] Just like this aforementioned study, Ahmad et al reported that treatment failure was the main factor associated with MDR-TB.[17] Treatment failure is mainly associated with poor adherence to treatment. In our study, patients who had irregular treatment were exposed to MDR-TB. This can be explained by the lack of systematic application of DOT (Directly Observed Treatment). DOT was not applied in 58.6% of the cases and in 17.2% of the controls. Taking anti-tuberculosis drugs in front of a health provider every day is an act of safety for the patient and those around him; indeed, there is an association between unsupervised drug intake and multidrug resistance (p=0.000).

Table 4. Therapeutic Characteristics associated with MDR-TB Cases Dakar, 2010-2016 in univariate analysis.

Therapeutic characteristics		Cases n (%)	Controls n (%)	OR 95% CI	p
Number of previous episodes of tuberculosis treatment	0	88 (52.1)	474 (93.5)	1	
	≥1	81 (47.9)	33 (6.5)	13.2 (8.3-21.0)	0.000
Previous treatment failure	No	126 (74.6)	503 (99.2)	1	
	Yes	43 (25.4)	4 (0.8)	42.9 (15.1-121.8)	0.000
Directly Observed Treatment	Sanitary	70 (41.4)	420 (82.8)	1	
	Non-sanitary	99 (58.6)	87 (17.2)	6.8 (4.7-10.0)	0.000
Irregularity of treatment	No	145 (85.8)	489 (96.4)	1	
	Yes	24 (14.2)	18 (3.6)	4.5 (2.4-8.5)	0.000

Table 5. Factors associated with multidrug-resistant tuberculosis, Dakar, 2010-2016 in multivariate analysis.

Factors		Cases n (%)	Controls n (%)	Adjusted OR (95% CI)	p
Age	Less than 15 or more than 59	20 (11.8)	99 (19.5)	1	
	[15-59]	149 (88.2)	408 (80.5)	0.7 (0.3-1.7)	0.468
Sex	Male	114 (67.5)	379 (74.8)	1	
	Female	55 (32.5)	128 (25.2)	0.9 (0.4-1.2)	0.105
Area of residence	Other	126 (74.6)	419 (82.6)	1	
	Peri-urban	43 (25.4)	88 (17.4)	1.8 (1.5-4.9)	0.024*
Diabetes	Non	163 (96.4)	502 (99,0)		
	Yes	6 (3.6)	5 (1.0)	1.3 (0.1-1.6)	0.114
Alcohol	No	165 (97.6)	505 (99.6)	1	
	Yes	4 (2.4)	2 (0.4)	1,5 (0.2-2.0)	0.235
History of multidrug-resistant Tuberculosis in the entourage of patient	No	145 (85.8)	505 (99.6)	1	
	Yes	24 (14.2)	2 (0.4)	7.0 (6.1-9.5)	0.002*
Number of previous episodes of tuberculosis treatment	0	88 (52.1)	474 (93.5)	1	
	≥1	81 (47.9)	33 (6.5)	1.4 (1.1-2.0)	0.321
Previous treatment failure	No	126 (74.6)	503 (99.2)	1	
	Yes	43 (25.4)	4 (0.8)	29.5 (27.3-30.1)	0.000
Directly Observed	Sanitary	70 (41.4)	420 (82.8)	1	
Treatment (DOT)	Non-sanitary	99 (58.6)	87 (17.2)	4.3 (4.1-7.2)	0.000
Irregularity of treatment	No	145 (85.8)	489 (96.4)	1	
	Yes	24 (14.2)	18 (3.6)	1.7 (0.5-5.4)	0.037

*Statistical significant.

Conclusions

Significant factors associated with the occurrence of the MDR-TB were: residing in a peri-urban area, presence of multidrug-resistant tuberculosis in the entourage of patient, previous treatment failure, treatment not directly observed (by a provider) and irregularity of treatment. Active search of MDR-TB cases in the patient's environment and adherence to the standard of care of sensitive tuberculosis would help prevent multiresistance.

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