MEDDOCS Open Access Publisher

ISSN: 2639-4391

Annals of Epidemiology & Public Health

Open Access | Research Article

Factors associated with multidrug-resistant tuberculosis in Guinea-Bissau from January 1, 2018 to December 31, 2019

Alberto Luis Papique+; Pauline Kiswendsida Yanogo[1,2]*; Nicolas Meda[1,2]

[1]Burkina Field Epidemiology and Laboratory Training Program, Joseph KI ZERBO University, Burkina Faso.

[2]Department of Public Health, Unit of training and research in Health science, University Joseph KI ZERBO, Burkina Faso.

***Corresponding Author(s): Yanogo Kiswendsida Pauline**

Department of Public Health, Unit of training and research in Health science, University Joseph KI ZERBO, Burkina Faso.

Email: y_poline@yahoo.fr & papique75@gmail.com

Received: Aug 30, 2021

Accepted: Nov 01, 2021

Published Online: Nov 03, 2021

Journal: Annals of Epidemiology and Public health

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Multidrug-resistant tuberculosis; Associated factors; Guinea Bissau.

Abstract

Background: Drug resistance to anti-tuberculosis drugs is a major public health problem that undermines successes in TB control. In Guinea-Bissau there were 25 MDR-TB patients in 2017 for an estimated treatment success rate of 44%. It is imperative to act at the grassroots level to prevent the emergence of such resistance, but no similar study has been carried out in the country. The objective of the study was to determine the factors associated with multidrug-resistant tuberculosis in Guinea-Bissau.

Methods: This unpaired case-control study included all multidrug-resistant tuberculosis (MDR-TB) cases and three controls for each case diagnosed between January 1, 2019 and December 31, 2019. We fitted an unconditional logistic regression model to determine the factors associated with MDR-TB.

Results: A total of 33 cases were included in the analysis. Prior treatment failure ORa = [14.93; 95% CI (5.22 - 42.64); p = 0.0001], knowledge of DOT strategy ORa= [5.23; 95% CI (2.14-12.80); p=0.0003], momentary interruption of treatment ORa= [5.26: 95% CI (1.88-14.75); p=0.0016] and failure to adhere medication times ORa = [0.18 95% CI (0.06-0.57); p=0.0033] were significantly associated with multidrug-resistant tuberculosis.

Conclusions: These results underline the need for adequate management of tuberculosis in Guinea-Bissau. The country would need substantial donor support to strengthen its diagnostic capacity for MDR-TB through the establishment of routine access to susceptibility testing and to strengthen its management capacity by subsidizing second-line drugs and training of medical specialists.

Cite this article: Papique AL, Yanogo PK, Meda N. Factors associated with multidrug-resistant tuberculosis in Guinea-Bissau from January 1, 2018 to December 31, 2019. A Epi demiol Public Health. 2021; 4(1): 1068.

Background

Drug resistance to anti-tuberculosis drugs is a major public health problem that undermines success in the fight against TB control. Each year, the number of new cases increases while treatment is successful for only 57% of MDR-TB patients. In 2019, 203,030 cases of multidrug-resistant or rifampicin-resistant TB were detected and reported globally, an increase of 10% compared to 2018 [1]. Drug resistance occurs when antibiotics are incorrectly prescribed, are of poor quality, or are prematurely discontinued by patients. MDR-TB affects all African countries except Seychelles. In 2016, between 36,000 and 44,000 cases of MDR-TB were recorded on the continent. In the West African sub-region, MDR-TB is an emerging problem. A study of tuberculosis cases detected between 2012 and 2014 in eight countries in this region found that 20% of new TB cases were MDR-TB [2]. Also, WHO estimates that approximately 68% of MDR-TB cases are diagnosed and that there is a gap between diagnosed and treated cases. In Guinea-Bissau, where the fight against MDR-TB is embryonic, a study conducted in 2012 estimated the prevalence of MDR-TB among patients admitted to TB treatment at 9% in 2012 [3].

In response to this disturbing situation, several strategies have been implemented by the WHO. The objectives of the most recent strategies adopted in 2015 have been revised upwards following the adoption of the new Sustainable Development Goals. Thus, by 2035, the WHO aims to reduce the number of deaths by 95%, the number of new cases by 90%, and to eliminate all the high costs in the management of tuberculosis [4]. For more efficiency, the WHO Africa Regional Office has developed a strategy implementation plan that is adapted to the realities of African countries [5]. Thus, the plan aims to reduce the number of deaths due to tuberculosis by 35%, the number of tuberculosis patients by 20% and the total elimination of the exorbitant costs in TB management by 2020. In 2016, the WHO adopted a new treatment protocol for non-drug-resistant MDR-TB patients with a shorter and standardized treatment regimen. The duration of treatment is twice as short as for conventional treatment, which lasts up to 2 years of treatment. At the same time, the WHO approved a rapid test for the diagnosis of MDR-TB and validated two molecules, bedaquiline and delamanid for the treatment of the disease [4].

Despite all of these efforts, MDR-TB statistics remain stable. The proportions of MDR-TB among new cases of TB, MDR-TB with a history of TB treatment and the ratio of MDR-TB with a history of TB / MDR-TB without a history of TB treatment were estimated at 3.36%, 17.8% and 4.6 respectively in 2019. The same statistics are respectively estimated at 3.32%, 17.7% and 4.2 in 2020 [4]. In addition, studies examining factors associated with MDR-TB conducted outside Africa and in Africa south of the Sahara have identified alcoholism [6], history of anti-TB treatment [7,8], interruption of treatment [7,9], smoking [7], frequent contact with an MDR-TB patient, rural residence, treatment failure, non-compliance with drug intake times [9] as factors associated with the onset of MDR-TB. No similar study has been conducted in Guinea-Bissau, where the active file of MDR-TB patients in the country numbered 25 patients in 2017 for an estimated treatment success rate at 44% [4]. Our research aims to fill this gap by studying the database of TB cases diagnosed and followed between January 1, 2018 and December 31, 2019 in Guinea. Our goal is to produce evidence that would contribute to better adapt the MDR-TB control strategy in Guinea-Bissau.

Methods

Study setting

The Republic of Guinea Bissau is a coastal country located in West Africa. It is bounded to the north by Senegal, to the southeast by Guinea and to the west by the Atlantic Ocean. The surface area of the country is 36,125 km². The country has 11 health regions subdivided into 116 health areas (the level closest to the communities), and 25 CDTs [10]. The National Tuberculosis Control Program (PNLT) was established in 1986 with the support of WHO and AIFO (Italian NGO specialized in the field of leprosy and tuberculosis). Its ability to intervene was undermined by the 1998-99 war; which led to the worsening of tuberculosis statistics and the advent of drug resistance. The DOTS strategy, implemented in 2002, is still in the implementation phase. It currently covers 4% of health structures. As of 2019, all TB diagnostic sites / laboratories using microscopy had a quality assurance procedure. Conversely, no laboratory using the GeneXPERT MTB/RIF technique, a gold standard for the diagnosis of MDR-TB in low risk MDR-TB countries [11], has such a procedure [4]. The Annual Risk of Infection (ARI), the incidence rate, the potential progression rate are respectively equal to 2.5%, 127/100,000 cases and 10% per year [10]. Cases of MDR-TB are rare there. In addition, between 40 and 50% of cases are HIV/TB coinfected patients. In 2017, 25 MDR-TB patients were followed up in the country [4].

Type and period of study

This is an unmatched analytical case-control study of multidrug-resistant tuberculosis cases in the 2018 and 2019 cohorts.

Study population

The study population consisted of patients diagnosed with bacteriologically confirmed pulmonary tuberculosis during the study period and who were followed up in the CDTs of the country's 11 health regions from January 01, 2018 to December 31, 2019.

Definitions

Is considered to be Case, any patient with pulmonary tuberculosis confirmed bacteriologically, having the result of the susceptibility test (TDS) or the GeneXpert TB-MR/RIF confirming infection with a Mycobacterium Tuberculosis resistant to at least Rifampicin, during the study period, contacted or seen and agreed to participate in the study. A control was any patient with bacteriologically confirmed cured TB (negative Epstein-Barr virus), who shares the same socio-demographic characteristics as the case during the study period, contacted or seen and accepted to participate in the study.

Sampling

Sampling was exhaustive for cases and simple random for controls at a ratio of 1 case for 3 controls.

Data collection procedure

The group of cases was obtained exhaustively from the database of multidrug-resistant tuberculosis cases registered at the Raoul Follereau Hospital, the only reference center to perform GeneXpert tests in the country. Three controls were selected for one case and controls were chosen in a simple random way from the CDTs of the health district of the case. After checking the tuberculosis registers in the health districts, the "random" function of Excel was used to select controls, whom were then

contacted by telephone for their availability and consent. Finally, a data extraction sheet was used to find controls for the administration of the questionnaire on factors associated with MDR-TB. These data were collected from the TB patient registry, laboratory records, patient files and by telephone interview.

MR Data processing and analysis

Case data were extracted from the Raoul Follereau Hospital database. The data of the controls, selected in the registers of the regional CDTs, were entered into the software Epi Info 7.2.2.6 on which an Excel database was created for the statistical analysis. The entered data was cleaned up by removing duplicates. In the descriptive analysis we proceeded to the description in time, place and person of the socio-demographic and clinical characteristics of the cases. Qualitative variables were described as a proportion with their 95% confidence intervals. Quantitative variables were described as a median with their range.

Univariate logistic regression was used to identify factors associated with MDR-TB. Then, variables associated with infection with a p <0.20 in univariate analysis were included in a stepwise descending multivariate logistic regression to look for factors independently associated with MDR-TB; adjusted OR with their 95%CI and p-value were calculated. Associations were tested by Fisher's Exact test. The significance level retained was $\alpha \leq 0.05$. Analyzes were carried out using the Epi-info software version 7.2.1.

Results

In total, we obtained 33 cases of MDR-TB and most cases 57.58% (n = 19/33) were diagnosed in 2019.

Sociodemographic and clinical characteristics of cases of multidrug-resistant tuberculosis in descriptive analysis, Guinea-Bissau, 2018 -2019.

The median age was 37 years with a minimum of 21 years and a maximum of 75 years. Male patients were the majority with a sex ratio M / F of 1.75. The majority of MDR-TB cases lived in urban areas (60.61%) and almost one in two households had less than 3 members (45.45%). Primary (27.27%) and secondary (27.27%) education levels predominated. Of the 33 MDR-TB patients interviewed in our study, 75.76% were non-civil servants. Common-law was the predominant marital status (63.64%). The majority of cases lived within 5 km of the CDT (63.64 (Table 1).

More than half of the cases (57.58%) have ever used tobacco and; two out of three patients (66.67%) reported consuming alcohol. More than three-quarters of patients (78.79%) of the cases had received special attention from family members during the treatment period. Almost as many as the aforementionned were not aware of the DOT strategy (75.76%). Most of the cases (87.88%) adhered to the time of taking medication and reported knowing the schedule for check-ups (87.88%). The vast majority of cases (93.94%) were well treated by health technicians. The majority (84.85%) had temporarily interrupted treatment mainly because of side effects (53.57%) or lack of food (50.00%). The majority (84, 85%) of the cases had a history of treatment failure for susceptible tuberculosis. Less than one in ten cases (7.06%) had a history or presence of MDR-TB in their family. Almost one-third (27.27%) had tested positive during the treatment period (Table 2).

Factors associated with MDR-TB in Guinea-Bissau, 2018 – 2019 in univariate analysis

In our univariate analysis, no socio-demographic characteristic was associated with multidrug-resistant tuberculosis.

In contrast, four clinical factors associated with MDR-TB in Guinea-Bissau knowledge of the DOT strategy [OR=5.2; 95% CI (2.14-12.80); p=0.0001], temporary interruption of treatment [OR=5.27; 95% CI (1.88-14.76); p=0.00027], treatment failure [OR=14.93; 95%CI (5.22-42.64); p=0.0001]. Finally, the adherence of the hours of medication taken was be a protective factor against MDR-TB [OR=0.18; 95% CI (0.06-0.57); p=0.0005] (Table 3).

Table 1: Sociodemographic characteristics of multidrug-resistant tuberculosis cases, Guinea-Bissau, 2018-2019.

Variables	Case n (%)
Sex	
Male	21 (63.64)
Feminine	12 (36.36)
Place of residence	
Urban	20 (60.61)
Rural	13 (39.39)
Number of people in the same household	
Less than 3	15 (45.45)
3 to 5	14 (42.42)
6 and more	4 (12.12)
Educational level	
Illiterate	7 (21.21)
Primary	9 (27.27)
Secondary	9 (27.27)
Pre-university	5 (15.15)
University	3 (9.09)
Occupation	
Official	8 (24.24)
Non-civil servant	25 (75.76)
Source of income	
Yes	17 (51.52)
No	16 (48.48)
Marital status	
free Union	21 (63.64)
Single	11 (33.33)
Divorced	0 (0.00)
Widowed	1 (3.03)
Distance between place of residence and CDT	
Less than 5 km	21 (63.64)
From 5 to 10 km	10 (30.30)
More than 10 km	2 (6.06)

Source: Register of TBMR cases at Raoul Follereau hospital 2018/19 and questionnaire

Table 2: Clinical characteristics of multidrug-resistant tuberculosis cases, Guinea-Bissau, 2018-2019.

Factors studied	Case n(%)
History of TB	
Yes	33 (100.00)
No	00 (00.00)
History of smoking	
Yes	14 (42.42)
No	19 (57.58)
History of alcohol consumption	
Yes	22 (66.67)
No	11 (33.33)
History of drug use	
Yes	2 (6.06)
No	31 (93.94)
Attitude of the family towards the patient	
Carefully	26 (78.79)
With mistrust	7 (21.21)
Knowledge of DOT	
Yes	25 (75.76)
No	8 (24.24)
Observance of medication times	
Yes	29 (87.88)
No	4 (12.12)
Knowledge of the timing of follow-up exams	
Yes	29 (87.88)
No	4 (12.12)
Assessment of the level of care in the CDT and health structure	
Good	31 (93.94)
Bad	2 (6.06)
Temporary interruption of treatment	28 (84.85)
Yes	28 (84.85)
No	5 (15.15)
Reason for interruption	
Side effects	14 (50.00)
Lack of food	15 (53.57)
Others	5 (17.86)
Treatment failure (previous treatment)	
Yes	28 (84.85)
No	5 (15.15)
Family history of MDR-TB	
Yes	2 (6.06)
No	31 (93.94)
HIV testing	
Yes	26 78.79)
No	7 (21.21)
HIV status	
Negative	17 (51.52)
Positive	9 (27.27)
Unknown	7 (21.21)
History of Diabetes	
Yes	2 (6.06)
No	29 (87.88)

Source: Register of TBMR cases at Raoul Follereau hospital 2018/19 and questionnaire

Table 3: Clinical factors associated with multidrug-resistant tuberculosis in Guinea-Bissau, 2018 - 2019, univariate analysis.

Factors studied	OR	95% CI	p-value
Attitude of the family towards the patient			0.37
With mistrust	1		
Carefully	1.18	0.40 -3.08	
Concept of TB in the family			0.40
No	1		
Yes	1.19	0.36-3.91	
Knowledge of DOT			0.0001
No	1		
Yes	5.2	2.14-12.80	
Observance of medication times			0.0005
No	1		
Yes	0.18	0.06-0.57	
Knowledge of the timing of follow-up exams			0.037
No	1		
Yes	2.71	0.87-8.45	
Temporary interruption of treatment			0.0002
No	1		
Yes	5.27	1.88-14.76	
Treatment failure (previous treatment)			0.0001
No	1		
Yes	14.93	5.22-42.64	
HIV testing			0.21
No	1		
Yes	0.66	0.24-1.98	
Knowledge of HIV status			1.92
No	1		
Yes	0.71	0.26 - 1.91	
History of Diabetes			0.37
No	1		
Yes	0.73	0.14 - 3.54	

Source: Register of TBMR cases at Raoul Follereau hospital 2018/19 and questionnaire

Factors independently associated with multidrug-resistant tuberculosis Guinea-Bissau, 2018 – 2019 in multivariate analysis

Table4 summarizes the factors independently associated with tuberculosis. In multivariate analysis, the factors that appeared independently associated with multidrug-resistant tuberculosis were prior treatment failure [ORa = 14.93; 95% CI (5.22-42.64); p = 0.0001], knowledge of the DOT strategy [ORa = 5; 23; 95% CI (2.14-12.80); p = 0.0003], momentary interruption of treatment [ORa = 5.26; 95% CI (1.88-14.75); p = 0.0016] and adherence to medication times [ORa = 0.18; 95% CI (0.06-0.57); p = 0.0033]; the latter was a protective factor against multidrug-resistant tuberculosis.

Table 4: Clinical factors associated with multidrug-resistant tuberculosis in Guinea-Bissau, 2018 - 2019, univariate analysis.

Variables	ORa.	95% CI	p-value
Previous treatment failure			0.0001
No	1		
Yes	14.93	5.22-42.64	
Knowledge of DOT strategy			0.0003
No	1		
Yes	5.23	2.14-12.80	
Temporary interruption of treatment			0.0016
No	1		
Yes	5.26	1.88-14.75	
Observance of medication times			0.0033
No	1		
Yes	0.18	0.06-0.57	

Discussion

Our study, which is the first in the country, was able to identify certain clinical factors associated with multidrug-resistant tuberculosis in Guinea-Bissau from January 1, 2018 to December 31, 2019. These were temporary interruption of treatment, previous treatment failure, knowledge of Directly Observed Treatment, Short-course (DOTS) strategy and non-compliance with medication times.

In our study, momentary interruption of treatment was a factor associated with multidrug-resistant tuberculosis. This result is similar to the result obtained by Misombo-Kalabela et al. [12] in his study on the risk factors for multidrug-resistant tuberculosis in the city of Kinshasa in the Democratic Republic of Congo in 2016; Ahmad et al, on the risk factors for multidrug-resistant tuberculosis in Pakistan. In fact the latter found that momentary interruption of treatment exposed fifteen times more to multidrug-resistant tuberculosis [13]. Ndiaye et al., on factors associated with multidrug-resistant tuberculosis in Dakar found that tuberculosis patients who interrupt their treatment had almost twice the risk of developing multidrug-resistant tuberculosis [14]. This can be explained by the fact that the treatment is extremely unpleasant, long and restrictive, and that little information is received from professionals.

In this study, patients who had a history of previous treatment failure were 15 times more likely to develop multidrug-resistant tuberculosis (OR = 14.9; 5.22-42.64; p = 0.0001). This result is in line with the the study of Misombo-Kalabela A, et al. on the risk factors for multidrug-resistant tuberculosis in the city of Kinshasa in the Democratic Republic of Congo where patients who had failed previous treatment had a six-fold increased risk of developing multidrug-resistant tuberculosis (OR = 5.5 95% CI 1.7-17.4). Skrahina et al. in Belarus showed that the previous treatment history for TB was the main independent risk factor for multidrug-resistant tuberculosis (OR = 6.1; 95% CI 4.8 - 7.7). Suárez-Garcia et al [15] and Lukoye et al. [16] also identified the history of treatment for tuberculosis as a factor associated with MDR-TB following a systematic review of research on MDR-TB in sub-Saharan Africa;

Our analysis also shows that knowledge of the DOTS strategy in the treatment of tuberculosis is a factor associated with multidrug-resistant tuberculosis. This result was contrary to that of the study conducted by Ndiaye et al. on factors associated with multi-drug resistant tuberculosis in Dakar [14], where patients who had treatment not observed directly by a health professional had four times the risk of developing multidrug-resistant tuberculosis. This fact could be linked to negligence on the part of health workers, lack of prior information to patients and unavailability of the family to follow the treatment. Indeed, these patients who will claim to know the strategy and its principles could lead health workers to trust them and not monitor their medication intake; which leads to non-compliance with the treatment schedule. The DOT strategy is only in its infancy in Guinea Bissau.

Patients who adhered to medication times during their first-line treatment appeared to be protected from multidrug-resistant tuberculosis. These observations corroborate those of Misombo-Kalabela A, et al. on the risk factors for multidrug-resistant tuberculosis in the city of Kinshasa in the Democratic Republic of Congo [12]. Tuberculosis patients who did not respect drug intake times during the first-line treatment did not seem to be protected against multidrug-resistant tuberculosis; which is logical in the sense that non-compliance with treatment is one of the conditions known to promote the development of resistance mutations [17].

The scope of our study is limited by the following reasons. First, we did not find some cases and other selected controls by what they had changed telephone contact for some cases and controls that could be due to them loosing their phones and SIM cards. Second, many patients did not get tested for HIV due to out-of-stock tests at CDTS and less likely to be requested by technicians.

The lack of proficiency in the local language (Fulani, Mandinka and Balanta) is also a limitation of our study.

Conclusions

Our study on the data from 2018 and 2019 identified that the failure of the previous treatment, the lack of knowledge of the DOT strategy and the temporary interruption of treatment as factors associated with multidrug-resistant tuberculosis in Guinea-Bissau. Adherence to the drug-taking times seemed to protect against multidrug-resistant tuberculosis.

Actions targeted at these factors, in particular improving public health education, intensifying the community DOT strategy for all tuberculosis patients, actively searching for cases and those lost to follow-up, ensuring regular follow-up of standardized treatment and adoption of the new short and effective treatment regimen would reduce this burden.

Furthermore, additional studies are needed to clearly establish the epidemiological link and causal relationships between the prior treatment failure, knowledge of the DOT strategy and the temporary interruption of treatment and the development of MDR-TB.

Declarations

Acknowledgements

We would like to thank the National tuberculosis control programm.

Ethics approval and consent to participate

We obtained approval of the Ministry of Public Health to conduct the study. All those included in the study were informed of the implications of their participation and were reassured that their informed consent were obtained. The confidentiality of the information collected was ensured by anonymity. A personal identification code was assigned. Verbal or written informed consent was obtained from both the case and the control groups before the questionnaire was administered. All electronic data were password protected. The result of this study will be used to improve treatment, prevention and control measures and to understand the magnitude of the problem of MDR-TB as a public health problem and to reduce the incidence of MDR-TB in Guinea-Bissau.

Consent to publish

Not applicable

Funding: This research did not receive funding

Availability of data and materials

Data are available on request to the following authors (Papique Alberto Luis and Yanogo Pauline Kiswendsida).

Competing interest

The authors declare that they have no competing interests

Authors' contributions

ALP conceived, designed, analyzed data; he wrote and prepared the final draft of the manuscript.

PKY contributed in the interpretation of results, in the writing and the finalization of the manuscript.

PKY, and **NM**: Provided comments on the study design and reviewed the manuscript.

All authors have read and approved the manuscript

References

1. Tuberculosis [Internet]. 2021.
2. Otu J, Gehre F, Zingue D, Kudzawu S, Forson A, et al. MULTI-DRUG-RESISTANT TUBERCULOSIS (MDR-TB): AN EMERGING PROBLEM IN WEST AFRICA. BMJ Global Health. 2017; 2.
3. Rabna P, Ramos J, Ponce G, Sanca L, Mané M, et al. Direct detection by the xpert MTB/RIF assay and characterization of multi and poly drug- resistant tuberculosis in Guinea-Bissau, West Africa. PLoS ONE. 2015; 10.
4. WHO. Global tuberculosis report 2020 [Internet]. 2020.
5. Tuberculosis (TB) | WHO | Regional Office for Africa [Internet]. [cité 4 juill 2021.
6. Skrahina A, Hurevich H, Zalutskaya A, Sahalchyk E, Astrauko A, et al. Multidrug-resistant tuberculosis in Belarus: the size of the problem and associated risk factors. Bulletin of the World Health Organization. 2013; 91.
7. Fregona G, Cosme LB, Moreira CMM, Bussular JL, Dettoni V do V, et al. Risk factors associated with multidrug-resistant tuberculosis in Espírito Santo, Brazil TT - Fatores associados à tuberculose resistente no Espírito Santo, Brasil. Rev saúde pública. 2017; 51.
8. Barroso EC, Mota RMS, Santos RO, Sousa ALO, Barroso JB, et al. Risk factors for acquired multidrug-resistant tuberculosis TT - Fatores de risco para tuberculose multirresistente adquirida. Jornal de Pneumologia. 2003; 29.
9. Ndiaye M, Yanogo PK, Sawadogo B, Diallo F, Antara S, Meda N. Factors associated with multi-drug-resistant tuberculosis in Dakar, Senegal, 2010-2016. J Public Health Afr. 2019; 10: 1099.
10. Ministère de la Santé: République de Guinée. Plan Directeur De Lutte Contre Les Maladies Tropicales Négligées En Guinée (2017- 2020).
11. WHO. Automated Real-Time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampicin Resistance: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children: Policy Update [Internet]. Geneva: World Health Organization; 2013.
12. Misombo-Kalabela A, Nguefack-Tsague G, Kalla GCM, Ze EA, Diangs K, et al. [Risk factors for multidrug-resistant tuberculosis in the city of Kinshasa in the Democratic Republic of Congo]. Pan Afr Med J. 2016; 23: 157.
13. Ahmad AM, Akhtar S, Hasan R, Khan JA, Hussain SF, et al. Risk factors for multidrug-resistant tuberculosis in urban Pakistan: A multicenter case–control study. International Journal of Mycobacteriology. 2012; 1: 137-142.
14. Ndiaye M, KiswendsidaYanogo P, Sawadogo B, Diallo F, Antara S, et al. Factors associated with multi-drug-resistant tuberculosis in Dakar, Senegal, 2010-2016. Journal of Public Health in Africa. 2019; 10: 1099.
15. Suárez-García I, Rodríguez-Blanco A, Vidal-Pérez JL, García-Viejo MA, Jaras-Hernández MJ, et al. Risk factors for multidrug-resistant tuberculosis in a tuberculosis unit in Madrid, Spain.
16. Lukoye D, Ssengooba W, Musisi K, Kasule GW, Cobelens FGJ, et al. Variation and risk factors of drug resistant tuberculosis in sub-Saharan Africa: A systematic review and meta-analysis. BMC Public Health. 2015; 15.
17. Rockwood N, Abdullahi LH, Wilkinson RJ, Meintjes G. Risk factors for acquired rifamycin and isoniazid resistance: A systematic review and meta-analysis. PLoS ONE. Public Library of Science. 2015; 10.