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Factors Associated with Confirmed Tuberculosis Treatment Outcome: A Hospital Study Cohort in Dakar, Senegal

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Abstract

Context: In order to break the chain of tuberculosis transmission, all diagnosed cases must be followed until the treatment is complete. Several factors influence the treatment outcomes, particularly in hospitals where care is provided for patients with the most severe cases.

Methodology: The purpose of this retrospective cohort study was to analyze the evolution of the treatment outcomes from 2011 to 2015 and identify factors associated with unsuccessful TB treatment. Tuberculosis cases confirmed by bacteriology and/or by Xpert-MTB/Rif test, being treated in the Department of Infectious and Tropical Diseases at Fann University Hospital in Dakar, were included. The trend Ch^2 test was used to measure the evolution of treatment outcomes from 2011 to 2015 and logistic regression for the identification of the factors associated with unsuccessful TB treatment.

Results: We collected 413 confirmed tuberculosis cases. The average age of patients was 38 ± 12 years and the sex ratio: 1.3. Most patients of the 46.4% cases were admitted to hospital. The average weight during the beginning of the treatment was 51 ± 10.8 kg. The isolated pulmonary TB represented 86.2%, followed by the multifocal TB 11.8%. Patients receiving retreatment were 8.2%. The HIV seroprevalence was 60.67%. Bacilloscopy confirmed tuberculosis in 75% of the cases and the Xpert-MTB/Rif test in 25%. From 2011 to 2015, the percentage of patients with successful TB treatment has increased from 47.4% to 69.3% (p=0.006). Lost to follow up patients have decreased from 18.4% to 7.4% (p=0.04). Unsuccessful TB treatment was associated to hospitalization at TB diagnosis (AOR=7.15; 95% CI: 4.23 – 12.10), low weight when starting the treatment (AOR=0.33; 95%CI: 0.14 – 0.77), and co-infection with HIV (AOR=2.07; 95% CI: 1.17 – 3.71).

Conclusion: Overall, progress has been made in monitoring patients who have been treated for tuberculosis. However, the favorable outcome percentage could be increased by improving the nutritional condition of patients and intensifying early screening and fighting against HIV infection.

Keywords: Tuberculosis; Confirmed; Treatment; Outcome

Introduction

Tuberculosis is one of the causes of death in the world. The Global Plan to end tuberculosis on the period of 2016-2020 is to reach 90% of individuals who need TB treatment, and to achieve at least 90% treatment success [1]. These targets are particularly important for the smear-positive pulmonary tuberculosis cases which are contagious and are responsible for the dissemination of the disease. The diagnosis of these forms improved during these past years with liquid cultures, new LED fluorescent microscopy and the advent of Gen-Xpert/MTB which helps identify *Mycobacterium tuberculosis* and test susceptibility to rifampicine [2,3].

In Senegal, the incidence of tuberculosis estimated by WHO is 139 cases per 100, 000 habitants. Among the 13, 660 cases detected in the population in 2017, 88% were bacteriological Pulmonary tuberculosis [4]. The Screening, the application of directly observed treatment and the follow-up care of the diagnosed cases are provided at the operational level by the 80 tuberculosis treatment centers (CDT), including Fann's department of infectious and tropical diseases (SMIT) of the national university hospital center (CHNU). Unlike the cases on care in health centers, the clinical presentations are more severe in hospitals. The purpose of this study was to analyze the evolution of treatment outcomes of confirmed tuberculosis cases from 2011 to 2015 and identify factors associated with unsuccessful TB treatment at a university hospital of Dakar in Senegal [5].

Methodology

Setting

We conducted this study in the Department of Infectious Diseases at Fann University Hospital in Dakar (Senegal). It has a Screening and

Treatment Centre of TB since 1988. All diagnosed patients are registered and monitored for treatment outcomes according to the recommendations of the National Tuberculosis Control Program (NTP). The treatment is directly observed for the hospitalized patients and then after the follow-up care will be done on an outpatient basis after discharge from the hospital. The dispensing of anti-tuberculosis drug is provided by a state-certified nurse, under the supervision of a doctor in charge

Study design and population study

Our hospital-based retrospective cohort study included all the bacteriologically confirmed (by microscopy or Xpert MTB/RIF assay or both) tuberculosis cases treated from 2011 to 2015.

Case definitions: A case is defined According to previous TB treatment received by the patient. TB cases were classified as a new case (A patient who has never had treatment for TB or who has taken anti-tuberculosis drugs for less than 1 month) or a retreatment cases (relapse cases, Treatment after failure, Treatment after default).

Treatment regimen: In Senegal, irrespective of TB localization, we used the five anti-tuberculosis first line drugs and the regimen depend on case definition. For the new cases, we administrated 2 months (Intensive phase) of rifampicin-isoniazid-pyrazinamide-ethambutol, followed by 4 months (Continuation phase) of rifampicin-isoniazid (2RHZE/4RH). Retreatment cases received for 2 months (intensive phase) rifampicin-isoniazid-pyrazinamide-ethambutol-streptomycin, followed by 6 months (Continuation phase) of rifampicin-isoniazid-pyrazinamide-ethambutol (2 RHZES/6RHZE).

TB treatment outcomes

Cured: A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture negative in the last month of treatment and on at least one previous occasion.

Completed treatment: A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.

Failure: A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.

Died:A TB patient who dies for any reason during the treatment

Lost to follow-up: A TB patient whose treatment was interrupted for 2 consecutive months or more.

Transferred out: This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit

Data Collection

Socio-demographic data (age, gender, residential district), clinical aspects (date of TB diagnosis, hospitalization or outpatient, weight at treatment initiation, form of TB (pulmonary TB, Extra-pulmonary TB and multifocal TB), type of TB confirmation (microscopy or Xpert MTB/RIF assay or both), HIV status (positive, negative or Unknown), treatment regimen (new cases/retreatment cases) and TB treatment outcomes were collected. Medical records, TB and hospital registers, NTP treatment cards were used to document the collected data.

Statistical Analysis

Data was analyzed using Epi-info 3.7.1 software and SAS Software version 9.3, Cary, NC, USA. Frequencies, means, standard deviations, were used to describe the population study. To identify factors associated with TB treatment outcome, we classified the patients in two groups. "Successful TB treatment" included cured or completed treatment and "Unsuccessful TB treatment" included treatment failure, lost to follow up, died or transferred out to another health facility. Firstly, we conducted univariate analysis. Association of unsuccessful treatment, epidemiological, clinical and biological features was identified using chi^2 test (categorical variables) and Student test (Continuous variables). The logistic regression was used for multivariable analysis. Independent variables from the univariate analyses were entered into the multivariable model if significant at $p<0.20$ level. Odds ratios (OR) were reported with a 95% Confidence Interval. A p value<0.05 was considered statistically significant in multivariable analysis.

Ethical Considerations

The Head of the Department of Infectious Diseases approved this retrospective study. All data collected were anonymized prior to analysis.

Results

Characteristics study population

We included 413 confirmed tuberculosis cases of which 91.8% new cases. The average age was 38 ± 12 years and the sex ratio 1.3. More than three-quarters of the patients (70.2%) came from the urban and suburban districts of Dakar region (Centre, North, South, Pikine) (Tables 1 and 2).

Variables	Number	Percent
Year of TB diagnosis		
2011	76	18,4
2012	70	17,0
2013	79	19,1
2014	93	22,5
2015	95	23,0
Sex		
Male	235	57,0
Female	178	43,0
Age group (years)		
15-44	292	70,7
45-60	93	22,5
>60	28	6,8
District residence		
Urban districts/Dakar region	264	64,2

Sub-urban districts Dakar region	132	32,1
Others regions	15	3,7
Hospitalization		
Yes	191	46,2
No	222	53,8
Weight at TB diagnosis (Kg)		
25-39	47	11,5
40-54	213	52,0
55-70	133	32,4
>71	17	4,1
Clinical presentation		
Pulmonary only	356	86,2
Multifocal	49	11,8
Extra-pulmonary only	8	2,0
Treatment category		
New cases	382	91,8
Retreatment cases	31	9,2
Confirmation of TB		
Microscopy	310	75,1
Xpert MTB/RIF assay	100	24,2
Both	3	0,7
HIV status		
Positive	199	48,2
Negative	129	31,2
Unknown	85	8,5
Outcome TB treatment		
Cured	187	45,3
Completed treatment	48	11,6
Died	72	17,4
Transferred out	57	13,9
Lost to follow up	48	11,6
Treatment failure	1	0,2

Table 1: Socio-demographic, clinical, and outcome description of study population.

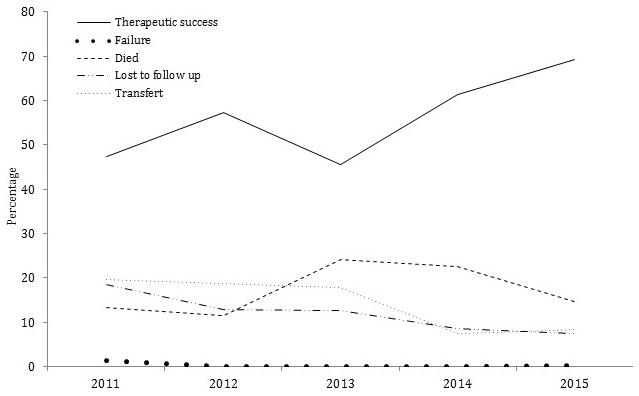

Figure 1: Evolution of the outcomes of 413 cases of confirmed tuberculosis treated at the Department of Infectious Diseases, Fann Hospital, Dakar, 2011-2015.

Variables	Number	Events* (n,%)	Crude OR (CI95%)	Ajusted OR (IC95%)**
Year of TB diagnosis				
2011	76	40 (52,6)	1	1
2012	70	30 (42,8)	0,67 (0,35 – 1,29)	0,74 (0,34-1,64)
2013	79	43 (54,4)	1,07 (0,57 – 2,02)	0,74 (0,33-1,63)
2014	93	36 (38,7)	0,59 (0,31 – 1,05)	0,38 (0,1-0,83)
2015	95	29 (30,5)	0,39 (0,21 – 0,74)	0,20 (0,08-0,46)
Sex				
Male	235	98 (41,7)	1	
Female	178	80 (44,9)	1,14 (0,77 – 1,69)	
Age group (years)				
15-44	292	115 (39,4)	1	1

45-60	93	50 (53,8)	1,79 (1,18 – 2,86)	1,43 (0,80-2,56)
> 60	28	13 (46,4)	1,33 (0,61 – 2,91)	1,51 (0,57-3,97)
District residence				
Urbain districts/Dakar	265	95 (36,0)	1	1
Sub-urbain districts/Dakar	132	70 (53,0)	2,00 (1,31-3,07)	1,40 (0,82 - 2,39)
Other sregions	125	12 (80,0)	7,11 (1,96-25,84)	4,29(0,92 - 19,98)
Hospitalization at TB diagnosis				
Outpatient	221	47 (21,2)	1	1
Inpatient	191	131 (68,5)	8,08 (5,18-12,60)	7,18(4,25-12,13)
Weight at TB diagnosis (Kg)				
25-39	47	28 (59,6)	1	1
40-54	213	103 (48,4)	0,63 (0,33-1,21)	0,53 (0,24-1,16)
55-70	133	41 (30,8)	0,30 (0,15-0,60)	0,34 (0,15-0,80)
>71	17	4(23,5)	0,21 (0,06-0,74)	0,26 (0,06-1,13)
Clinical presentation				
Pumonary only	356	144 (40,4)	1	1
Extra-pulmonary only	8	4 (50,0)	1,47 (0,36-5,98)	1,98(0,37 - 10,53)
Multifocal	49	30 (61,2)	2,32 (1,26-4,29)	0,88 (0,41 – 1,83)
HIV status				
Negative	129	40(31,0)	1	1
Positive	199	104(52,3)	2,43 (1,53-3,89)	2,01(1,17 - 3,60)
Unknown	85	34(40,0)	1,48 (0,83-2,63)	1,34 (0,66 – 2,75)
Treatment category				
New cases	382	158 (41,3)	1	1
Retreatment cases	31	20(64,5)	2,58 (1,20-5,53)	1,51(0,61 - 3,77)

*Unsuccesfull TB treatment; CI95%: 95% confidence interval; **AOR : Adjusted Odds ratio

Table 2: Factors associated with unsuccessful TB treatment outcome (n=413).

Among the 413 cases, 191 (46.4%) were hospitalized during the TB diagnosis. The average weight during the beginning of the anti-tuberculosis treatment was of 51 kg ± 10.8 kg. The isolated pulmonary tuberculosis was the most frequent (86.2%), followed by the multifocal tuberculosis (11.8%). The lymph node (7.4%) and neuro-meningeal (5%) localizations were the predominant extra-pulmonary forms.

313 cases of TB were confirmed by microscopy and Gen-Xpert test was positive in 100 patients. No Rifampicin resistant was detected. Gen-xpert was predominantly positive for pulmonary specimens (96 cases), the cerebrospinal fluid (LCR) (10 cases; 9.7%) and the lymph node puncture fluid (8 cases; 7.7%). The HIV seroprevalence was 48.2%. The cotrimoxazole prescription rate among the TB/HIV co-infected patients was 88.9% and almost one third was on antiretroviral treatment (30.7%) during hospitalization.

Tuberculosis treatment outcomes (Figure 1)

In our study, 235 cases (56.9%) had a successful TB response (cured or completed treatment). From 2011 to 2015, the percentage of patients increased significantly from 47.4% to 69.3% (p=0.006). The lethality was 17.4% and 11.6% of cases lost to follow up during TB treatment. In addition, the rate of patients lost to follow-up decreased progressively over the last 4 years from 18.4% to 7.4%, a drop of 61% (p=0.04). However, lethality did not progress (p=0.33).

Factors associated with unsuccessful TB treatment (Table 2)

By univariate analysis, the unsuccessful TB treatment was lower in 2015 in comparison with 2011 (crude OR=0.39; 95%CI: 0.21-0.74). Whereas, the treatment failure risk was increasing along with the age (45 – 60 years versus 15-44 years) (crude OR=1.79; 95%CI: 1.18 –

2.86). It was higher among patients residing in suburban area (crude OR=2.00; 95%CI: 1.31-3.07), and outside Dakar (crude OR=7.11; 95% CI: 1.96-25.84). The risk of unsuccessful TB treatment was decreasing when the weight was increasing during the beginning of TB treatment. By univariate analysis, the other factors associated with unsuccessful TB treatment were hospitalization during tuberculosis diagnosis (crude OR=8.08; 95%CI: 5,18-12.60), HIV infection (crude OR=2.43; 95%CI: 1.53-3.89), presence of a multifocal TB (crude OR=2.32; 95%CI: 1.26-4.29) and the previous TB treatment (crude OR=2.58; 95%IC: 1.20-5.53).

By multivariate analysis, the unsuccessful TB treatment was higher in 2011 in comparison with the years of 2014 (adjusted OR=0.38; 95%CI: 0.17-0.83), and 2015 (adjusted OR=0.20; 95%CI: 0.08-0.46), among the hospitalized patients at TB diagnosis (adjusted OR=7.18; 95%CI: 4.25 – 12.13) and in case of HIV infection (adjusted OR=2.01; 95%CI: 1.17-3.60). Moreover, the treatment failure risk was lower among patients with a weight of 55-70 kg during the beginning of the treatment in comparison with those with a weight between 25-39 kg (adjusted OR=0.34; 95%CI: 0.15-0.80).

Discussion

This study done at the hospital level in a Dakar environment confirms once again the importance of Gen-xpert in the tuberculosis diagnosis. About a quarter of the cases (24.9%) has been confirmed by means of its application. It was mainly positive among the pulmonary tests (93.2%). These data comply with the literature data. Steingart KR found again a sensibility (Se) of 89% [85%-92%] and a specificity of 99% [95%-99%] of Gen-Xpert for the pulmonary tuberculosis diagnosis with a difference according to the microscopy results (Se: 89% [85% – 92%] Microscopy (+) and Se: 67% [60% – 74%] Microscopy (-) [6]. However, the sensibility of Gen-Xpert is variable at the extra-pulmonary localizations: 50.9% in pleural fluid, 71.1% in the cerebrospinal fluid and 82.7% in the urine [7]. In our cases, it is mainly positive in the cerebrospinal fluid (9.7%) and the lymph node fluid (7.7%).

Concerning the outcome of patients, even if we have noticed a significant increase percentage of patients with successful TB treatment from 2011 to 2015 (47.4% to 69.3%, p=0.006), that rate remains low. These results are mainly related to the high prevalence of HIV infection (48.2%) and the high percentage of hospitalized patients (46.4%) in our cohort. The unsuccessful TB treatment was associated to hospitalization at TB diagnosis (AOR=7.15; 95%CI: 4.23 – 12.10) and co-infection with HIV (AOR=2.07; 95%CI: 1.17 – 3.71). These results are similar to those of Amante TD in Ethiopia (OR=2.5; 95%CI: 1.34 – 5.7) [8]. Excess mortality of co-infected patients has been clearly demonstrated. Most of the studies agree on the negative impact of HIV upon successful TB treatment among the tuberculosis patients [9,10] in relation to immuno-suppression presentation, the presence of other opportunistic infections and the complexity of the co-administration of anti-tuberculosis and antiretroviral treatment. Only one third of our patients were on antiretroviral treatment, this is due to the fact that some of them died, disappeared or were transferred out before being on treatment. In some cases, the application of antiretroviral therapy has not been notified to the nurse in charge of the treatment.

In our series, the proportion of lost to follow-up patients was high (11.6%). Comparable data were reported from Morocco by Hassani (10.3%) [11,12] and Diallo from Mali (17.4%) [13]. Previous history of tuberculosis, occurrence of side effects, family problems, and stigmatization has been reported as causes of treatment interruption. Continuous decline of the lost to follow-up patients rate (18.4% to 7.4%, p=0.04) noticed in our study due to the work of the social services department must be maintained. The National Tuberculosis Control Program is recommending that a patient should be sent to the health facilities close to the patient residence in order to lower the transport cost that may help to decrease the rate of the lost to follow-up patients.

By multivariate analysis, the unsuccessful TB treatment was more important in 2011 in comparison with the years of 2014 (AOR=0.38; 95%CI: 0.17 – 0.83) and 2015 (AOR=0.21; 95%CI: 0.09 – 0.49). This is comparable to the results of Fahrettin T [10] who had noticed a successful TB treatment increase from 73.8% between 1999 and 2002 to 83.6% between 2002-2004. In a study conducted in South Africa, the same trend was found again with a drop of 1.7% of treatment failures between 2003 and 2012 [14]. This is evidence of the efforts made during these last few years in the eradication of tuberculosis with the application of DOTS.

Indeed, this strategy aims to strengthen adherence to anti-tuberculosis treatment. If it is effectively applied, it will help to prevent the occurrence of new multidrug-resistant cases.

The relation between successful TB treatment and gender has not been noticed. But, some studies had pointed out that correlation [15]. In Africa, it is recognized that women have more access to health care services but nevertheless their active lives can have a negative impact on the treatment adherence.

Contrary to the findings of Kigozi, South Africa Gen who had noticed a low failure rate in older patients (p<0.001) [14], difference in terms of age has not been found in your study.

A positive association has been found between unsuccessful TB treatment and low weight at the beginning of the anti-tuberculosis treatment (AOR=0.33; 95%CI: 0.14 – 0.77). Likewise, Lackey [16] had found that the rate of successful TB treatment was more frequent in patients with body mass index>18.5 kg/m2 (OR 2.08; 95%CI: 1.21-3.56). Many researches have shown that malnutrition is a factor of poor prognostic [17,18]. During HIV infection, malnutrition is mostly the secondary opportunistic cause of digestive infections such as the oropharyngeal candidiasis, the infectious diarrhea.

By multivariate analysis, there was not a correlation between successful TB treatment and treatment regime. On the other hand, researchers have reported that patients on treatment were more in treatment failure risk [19,20] and that might be related to the emergence of strains resistant to the treatment.

Conclusion

Although there is a significant increase in the rate of successful TB treatment for confirmed tuberculosis patients, improved is still needed to achieve the 90% successful treatment rate. The recommendation actions are early application of the antiretroviral therapy and the improvement of patient's nutritional condition since the main two factors that influence the treatment and make the treatment unsuccessful are HIV infection and low weight during the beginning of the treatment.

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