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# **Research Article**

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# Epidemiological profile of pulmonary tuberculosis relapse cases in the city of Butembo east of the democratic republic of Congo

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#### **Abstract**

Introduction: Antibiotic resistance to the treatment of Tuberculosis is of growing concern around the world. The aim of this work was to determine the frequency and epidemiological factors of Tuberculosis relapse in Butembo town. Method: This descriptive study covered the period from January 1, 2005 to December 31, 2015. The research data were collected from the quarterly reports of the Tuberculosis Screening and Treatment Centers (TCSCs) in Butembo City. Data analysis was performed using Chi square, Odds Ratio and Linear Regression tests. Result: In a cohort of 4881 patients followed up for pulmonary tuberculosis in Butembo town, the frequency of Tuberculosis relapses was 1.78%. This frequency had an annual downward trend of -0.134%. The mortality rate for Tuberculosis relapses was 10%. History of alcohol and tobacco, associated morbidities such as HIV AIDS, malnutrition and diabetes were found to be significant risk factors for TB relapse. The onset of TB relapses was significantly dependent on the patients' profession. Conclusion: The trend of relapse cases is decreasing in Butembo City. This is in agreement with WHO's goals of reversing the epidemiological trend of Tuberculosis by 2020.

Keywords: Epidemiology, Tuberculosis, Relapse, Butembo.

#### INTRODUCTION

Tuberculosis is a major public health problem in the world. It is an infectious disease with a high epidemiological burden and represents a serious Public Health challenge <sup>[1]</sup>. It has been possible for more than 100 years to identify, through the microscope, the causative agent of tuberculosis "Mycobacterium tuberculosis". Effective TB drugs have been around for more than 50 years, and despite advances in treatment and prevention, TB continues to claim victims and the number of cases is increasing <sup>[2]</sup>.

Resistance to antibiotics used for the treatment of tuberculosis is of increasing concern worldwide [3, 13].

The World Health Organization (WHO) estimates that 650,000 people contract each year a strain of TB that is resistant to at least two important antibiotics, Isoniazid and Pyrazinamide. This refers to what is known as multidrug-resistant tuberculosis (MDR-TB) [3].

In low- and middle-income countries, MDR-TB cases are particularly problematic and common. This is due to prescription or administration errors, lack of absorption, or temporary interruption of tuberculostatics supply [4].

Researchers at the University of Alberta reviewed health data for MDR-TB cases identified between 1981 and 2011 among Canadian-born residents; the prevalence of MDR-TB rose from 0.65% to 2.11% [4].

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Tuberculosis case management can be an expensive burden for hospitals and clinics, and treatment is often uncomfortable for those affected due to its long-lasting course and in some cases drugs include parenteral antibiotics [4].

A person diagnosed with tuberculosis may include either one of the following: new case, relapse, treatment failure, treatment after interruption (discontinuation) or chronic case. Detection of the case by the health staff is an essential step that allows the individual to choose an effective therapy, minimize side effects and reduce the risk of resistance development. The case definition serves also as the basis of patient registration and case reporting [4].

A 1999 to 2005 retrospective study of 32 cases of relapsed pulmonary tuberculosis confirmed in low-income patients in Casablanca, Morocco, reported a high prevalence of relapse cases in young men, 66% in the average age 39 years. Smoking, diabetes, history of pulmonary tuberculosis, HIV infection are key determinants of relapse <sup>[5, 15]</sup>.

HIV-infected patients co-infected with TB are about 10 to 20 times more likely to relapse than non-HIV infected people. According to a Haitian study, the relapse rate for TB disease is 4.8 per 100 person years in the HIV-positive subject compared to 0.4 per 100 person-years in non-HIV-infected people, this corresponds to a relative risk relapse rate of 10.7 for HIV-positive patients <sup>[6]</sup>.

Bacterial resistance is the main obstacle to correct management and it is a major challenge in the fight against tuberculosis <sup>[7]</sup>. It is especially common in developing countries like the Democratic Republic of Congo <sup>[8]</sup>

Although this phenomenon is well known, studies analyzing the causes of relapse and resistance of tuberculosis remain rare <sup>[9]</sup>. Thus, we aimed to contribute to TB control in the city of Butembo. Specifically, this research consisted in determining the frequency of cases of relapse of pulmonary tuberculosis and its development in the city of Butembo from January 1st, 2005 to December 31st, 2015, and identifying the epidemiological characteristics of the subjects having experienced the relapse of tuberculosis.

# MATERIAL AND METHODS STUDY FRAMEWORK

This research was carried out in the Tuberculosis Screening and Treatment Health Centers (CSDT) in Butembo City, located in the two health zones, Butembo and Katwa. The health zone of Butembo runs four CSDTs two of which our study was conducted in: the CSDT of Kitatumba and the CSDT Makasi. The Katwa Health Zone has 3 CSDTs: Katwa CSDT, Matanda CSDT and Heshima Letu CSDT and both were included in our study.

# **Study Population and Sample**

This study looked at all the cases of pulmonary tuberculosis detected, patients aged 15 years and above, treated and registered in the Butembo Screening and Treatment Health Centers selected by this study. The subpopulation included any patient who developed pulmonary bacillifera tuberculosis, screened in the selected screening center, declared cured and whose relapse was confirmed by paraclinical examinations (Ziehl sputum, Gene Xpert if possible).

#### **METHODOLOGY**

This study was descriptive covering 11 years, from January 1st, 2005 to December 31st, 2015. We used the quarterly reports of the Butembo City CSDTs and the patient files.

The study variables were:

- Sociodemographic variables: the profession.
- Risk factors: HIV / AIDS, malnutrition, diabetes, smoking and alcoholism.

The data were processed by the software epi info 7, with the dependency tests Chi-square, Odds Ratio and Linear Regression using the following formula:

$$X_{cal}^2 = \sum \frac{\left(f_o - f_{th}\right)^2}{f_{th}}$$

 $\alpha_{0.05}$  = significant threshold (p-value)

$$OR = \frac{ad}{bc}$$
 OR= Odds Ratio

The OR confidence interval was calculated using Wolf's direct method. An association between a factor and TB relapse is established when OR is greater than 1. This association is considered significant when the OR confidence interval does not contain 1; otherwise, the association is not significant. The linear regression Y = a + bx stands for the function "frequency of tuberculous relapses" as a function of time "x"; b is the angular coefficient expressing the variation of the function y in a unit of time (year).

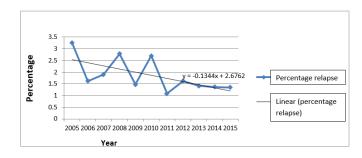
#### **RESULTS**

#### 1. Frequency of TB relapses

The results presented in this section concern 4881 tuberculosis patients followed in the different CSDTs of the city of Butembo. Data analysis found out that the frequency of relapse of pulmonary tuberculosis was 87 cases out of a total of 4881 tuberculosis patients, a rate of 1.78%. Of the cases of relapse, 46 were declared cured, ie 53%; 24 died corresponding to a mortality rate of 10%. The others are either lost for the follow up or transfered cases without retro-information data.

#### **Trends in Annual Frequencies of Tuberculosis Relapse**

Figure 1 shows the trend of TB relapses during the years 2005 to 2015



**Figure 1:** Evolution of the frequencies of Tuberculosis relapses according to the years.

The annual trend of TB relapses is down 0.134%

# 2. Tuberculosis relapse and patient history.

The following table lists patients with Tuberculosis relapses according to their previous addiction history: tobacco and alcohol.

**Table 1:** Distribution of Tuberculosis Relapse Cases according to patient history

Antecedent	Total TBC	Relapse	%	OR	Lower Lim	Upper Lim	X²	Degree of freedom
Smoking	930	31	3, 33	2,40	1,50	3,82	-	-
Alcohol	951	29	3,04	2,10	1,30	3,37	-	-
No smoking nor alcohol	3000	27	0,90	0,28	0,17	0,45	-	-
Total	4881	87	1,78	-	-	-	34,84	2

The history of smoking and alcoholism is significantly associated with TB relapse.

## 3. Tuberculosis relapse and Occupation

The following table lists cases of Tuberculosis relapse in relation to their occupations.

 Table 2: Distribution of Tuberculosis Relapse Cases by Occupation

Profession	Total TBC	Relapse TBC	%	OR	Lower Lim	Upper Lim	X <sup>2</sup>	Degree of freedom
Military	118	15	12,71	9,48	5,03	17,66	-	-
Clerks	71	2	2,81	1,61	0,00	6,83	-	-
Households	690	16	2,31	1,38	0,77	2,45	-	-
Farmers	1528	28	1,83	1,04	0,65	1,63	-	-
Unemployed	638	8	1,25	0,67	0,33	1,39	-	-
Dealers	846	6	0,92	0,35	0,14	0,83	-	-
Students(High school and graduate)	690	7	0,86	0,53	0,22	1,19	-	-
Teachers	300	5	0,55	0,93	0,33	2,40	-	-
Total	4881	87	1,78	-	-	-	91,55	7

The military profession is significantly associated with Tuberculosis relapse.

# 4. Tuberculosis relapse and associated pathologies

The following table lists the cases of tuberculous relapses according to the pathologies associated or the patient's field.

 Table 3: Distribution of tuberculous relapse cases according to the associated pathologies

Terrain	Total TBC	Relapse TBC	%	OR	Lower Lim	Upper Lim	X <sup>2</sup>	Degree of freedom
Malnutrition	81	12	14,80	10,96	5,39	21,87	-	-
Diabetes	300	18	6,00	4,17	2,36	7,30	-	-
HIV/AIDS	840	38	4,52	3,86	2,46	6,06	-	-
Others	3660	19	0,51	0,09	0,05	0,15	-	-
Total	4881	87	1,78	-	-	-	178,50	3

Malnutrition, diabetes mellitus and HIV infection are the pathologies that are significantly associated with TB relapse. NB: Others include:.....

# DISCUSSION

## 1. Frequency of TB relapses

The frequency of relapses of pulmonary tuberculosis during the years 2005 to 2015 in the city of Butembo is 1.78%. This rate is lower than that found in Mayotte, and those observed in Madagascar (6%), the Republic of Comoros (7.5%)  $^{[10]}$  and the Vietnam (8.6%, 95%CI 5.4–13)  $^{[14]}$ . This low frequency is due to the implementation of the National Tuberculosis control program and the adequate management of cases detected in Butembo City. The regression line of annual frequencies of Tuberculosis cases in Butembo City is decreasing with the angular coefficient b = -0.134 (Fig1). This decline is also globally observed along with the incidence of tuberculosis since the 2000s giving a total and overall decrease of 18%  $^{[11]}$ . This regression would be explained by efforts to implement the Millennium Development Goals (MDGs), which emphasize the provision of effective diagnostic and treatment tools to enable the control of Tuberculosis and the reverse of the trend before year 2015  $^{[11]}$ . In the latest WHO report, it is emphasized that

the global goal is to end the epidemic by 2016. The strategy aims to end the TB epidemic, reduce the incidence by 80% and Tuberculosis mortality by 90% and eliminate catastrophic expenditures for affected families by 2030  $^{[11]}$ .

## 2. Tuberculous relapse and patient history.

With a calculated Chi square of 34.84 which is greater than tabular Chi square (7.82), Table I shows a dependence between the onset of Tuberculosis relapses and the history of alcohol and tobacco. The consumption of alcohol exposes the patient significantly 2.40 times to relapse, followed by smoking which significantly exposes them 2.10 times. These results are consistent with the proven link between tobacco and Tuberculosis; with high mortality and a high risk of Tuberculosis relapse in smokers <sup>[5]</sup>. From a pathophysiological point of view, tobacco through its irritating effect on the respiratory tract influences mechanisms of local immune defense <sup>[2, 5]</sup>. Abuse of alcohol can have a negative impact on the nutritional status of the individual, thus promoting an immune decline.

#### 3. Tuberculous relapse and Occupation

From Table II, calculated Chi square (97.55) being greater than tabular Khi square (14.07) at degree of freedom of 7, it appears that there is an association between the profession and the occurrence of Tuberculous relapse. This has been actually observed for the military profession which exposes patients significantly 9.48 times to TB relapse than other professions. The reason is that they would have a high percentage of HIV co-infection and live promiscuous in their camps.

#### 4. Tuberculous relapse and associated pathologies

Since calculated Chi square (178.50) is far superior to tabular Chi square (5.99) at degree of freedom of 2, Table III shows a strong dependence between the associated pathologies (patient's ground) and the occurrence of Tuberculosis relapses. In case of TB disease, patients with malnutrition have significantly 10.96 times the risk of relapse, followed by diabetic patients who have 4.17 times and those infected with HIV 3.86 times. This later finding supports the view that decreased immunity is a key determinant of TB relapse in HIV infections. In fact, HIV-induced immunodeficiency increases the risk of TB relapse [12] and increases TB-related mortality by the following two mechanisms [6]: increasing susceptibility to new infections, allowing the infection to progress rapidly to clinical disease and allowing pre-existing latent TB infection to progress to clinically overt disease.

# CONCLUSION

Special attention should be paid to alcoholics, tobacco users, people living with HIV, malnourished people, people with diabetes and the military as they are the most at risk for TB relapse.

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