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Original Research Article

Factors associated with delayed diagnosis of pulmonary tuberculosis with positive bacilloscopy in Bangui, Central Africa

Jean de Dieu Longo[1]*, Henri Saint Calvaire Diemer[1], Sylvain Honoré Woromogo[2], Herman Doyama-woza[1], Gaby Ferreol Melkisedeck Gotia-Dondoumba[1], Gérard Grésenguet[1]

[1]Public Health Department, Faculty of Health Sciences, [2]School of Human and Veterinary Sciences, University of Bangui, Central African Republic

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***Correspondence:**
Dr. Jean de Dieu Longo,
E-mail: jeandedieulongo@gmail.com

ABSTRACT

Background: A case of untreated bacteriologically confirmed pulmonary tuberculosis (BPT+) represents a reservoir for transmission of the disease. The objective of this study was to evaluate the delay and identify the determinants of the delay in the diagnosis of BPT+ in the diagnostic and treatment centers for tuberculosis (CDT) in Bangui.
Methods: An analytical cross-sectional survey was conducted. It included all new TB patients aged 15 years and older (145) who presented a positive bascilloscopy. Exhaustive recruitment was performed during the study period. Multiple logistic regression with OR (95% CI) for $p<0.05$ was used to establish the relationship between delayed diagnosis and patient characteristics.
Results: Patients ranged in age from 16 to 80 years with an average age of 33.81±12.18 years. The time to consultation and diagnosis >30 days after the onset of symptoms were 83.10% and 23.95%, respectively. In multivariate analysis, male patients [ORa=0.42 (0.19-0.93)]; patients residing in peri-urban areas [ORa=4.25 (2.10-9.02)]; patients using informal care facilities as first option [ORa=1.84 (1.47-3.38)] and not requesting acid-fast bacilli (AFB) test at first visit [ORa=6.09 (3.70-17.69)] were associated with risk of delayed diagnosis.
Conclusions: Early diagnosis and treatment of BPT+, which is the spreading form of the disease, remains a public health concern in our context. Supervision and coaching of health workers coupled with increased public awareness of TB will contribute to better control of the disease.

Keywords: Bacilloscopy, Central Africa, Diagnostic delay, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is endemic in the Central African Republic. It is the most frequent opportunistic disease during HIV infection. The HIV-TB co-infection rate is estimated at 38.98%.[1] Despite the efforts made in relation to previous years, the objectives of screening 70% and curing 85% of cases set by the "stop TB" strategy adopted by the country have not been achieved. In addition, there are still problems of stigmatization, forced displacement of people due to conflicts and natural disasters, which leads to promiscuity in makeshift camps and families, especially in the peri-urban areas of Bangui.[2] Furthermore, the emergence of COVID-19 pandemic threatens to reverse recent progress in reducing the burden of tuberculosis. According to the World Health Organization (WHO), globally, the number of TB deaths could increase by approximately 200-400,000 in the year 2020.[3] Therefore, developing innovative control strategies, especially for bacillus-positive pulmonary tuberculosis (BPT+), which is the main source of dissemination of the infection in the communities, is crucial. In developing countries, undetected BPT+ patients are estimated to have the potential to infect 10-15

people per year and more than 20 during the natural history of their disease.[4] Therefore, better control of the disease in this setting relies mainly on the early detection and correct treatment of pulmonary forms of TB.[3,5]

However, despite global efforts to control TB, delay in diagnosis and initiation of treatment remains a major problem in many countries.[3,6] Delays in diagnosis and initiation of TB treatment are life-threatening for patients.[1,7]

In Central African Republic (CAR), data on delays in pulmonary tuberculosis diagnosis are not known. Knowledge of these delays and their determinants on a representative sample of BPT+ patients could help to formulate proposals for a better management of tuberculosis patients. This study was conducted to assess the time to diagnosis and to identify factors contributing to the delay in the diagnosis of BPT+ in the tuberculosis diagnostic and treatment centers (CDT) in Bangui.

METHODS

Study setting

We conducted this study in ten CDTs located in the three health districts of health region 7, which corresponds to Bangui city. These facilities were chosen because they receive all patients diagnosed with tuberculosis in the city of Bangui and its surroundings.

In 2021, Bangui had a population of 1,100,374 inhabitants, which representing 20% of the total population of the country, with a density of 15,812 inhabitants per km². The tasks of the CDTs include registering patients diagnosed with tuberculosis, providing free anti-tuberculosis treatment, following up tuberculosis patients at home, actively searching for irregular and lost patients and contact cases of BPT+ patients, referring suspected tuberculosis patients to the CDTs and sensitizing the population on tuberculosis.

Study design and period

This was an analytical cross-sectional study including all new cases of BPT+ registered in Bangui's tuberculosis diagnostic and treatment centers (CDT) from July 1 to September 30, 2021.

Inclusion and exclusion criteria

We included after informed consent, all new BPT+ cases aged at least 15 years diagnosed during the study period. Patients with BPT+ for whom data on time to diagnosis were not available were not included.

Study population and sampling

All patients with tuberculosis, aged 15 years and older, followed up in the CDTs selected for the study were included. We opted for an exhaustive recruitment. All patients who met the selection criteria during the study period and who consented were included.

Variables

Dependent variable

The time interval between the onset of the first symptoms, diagnosis and management is the dependent variable. These time intervals and delays are defined for each study participant as follows:

Time to diagnosis

The time from the onset of symptoms to the first visit to a healthcare provider. It was considered short when it was 1 to 14 days, medium when it was 15 to 29 days, and long when it was more than 30 days.

Time to treatment

The time from the first visit to a healthcare provider to the initiation of treatment. It was considered short when it was 1 to 14 days, medium when it was 15 to 29 days, and long when it was more than 30 days.

Total time

This is the time from the onset of the first signs to the initiation of treatment. It is the result of the sum of the two delays mentioned above. It was considered short when it was 15 to 29 days, medium when it was 30 to 59 days and long when it was more than 60 days.

Independent variables

Independent variables were represented by sociodemographic, clinical and paraclinical data, and factors of diagnostic delay.

Formal structures

These were defined as the healthcare facilities recognized by the health system.

Informal structures

These were defined as the healthcare facilities not recognized by the health system.

Data collection and analysis

We visited all the CDTs to collect data. Data collection was done by interviewing the patients who came to the appointments, using an anonymous survey form established beforehand. Data design and data entry were performed with Epi-data version 3.1. After data entry, we

proceeded to the data cleaning which allowed us to eliminate the outliers.

Data analysis was performed using Epi-Info version 7 software. We used the Chi square test of independence for comparison of proportions in cases of crosses between two categorical variables, with a significance threshold α =5% (0.05). Associated factors were identified first by bivariate analysis between the dependent and independent variables. Then, multivariate analysis using the binary logistic regression model with successive stepwise descending iterations of all variables with significance ≤0.20 in bivariate analysis was performed. Measures of association were estimated by odds ratio (OR) and their 95% confidence interval (CI). A p<0.05 was considered statistically significant.

Ethical considerations

The study received ethical clearance from the ethics and scientific committee (ESC) of the faculty of health sciences (FACSS). The study was carried out in strict compliance with the Declaration of Helsinki, which states that no intervention that could alter the dignity, integrity and right to privacy of the participants was carried out. Verbal consent was obtained from each patient prior to the interview and completion of the questionnaire. Each patient was assured that his or her refusal would not affect his or her treatment. The data were treated with strict confidentiality.

RESULTS

Socio-demographic characteristics of the patients

During the study period, 142 patients with BPT+ were included, which represents 27.2% of all registered TB patients. Mean age was 33.81±12.18 years with extremes of 16 and 80 years. The age range of 16 to 36 years was the most represented (69.72%). The male sex predominated (60.56%) with a sex ratio of 1.5. Three out of four respondents had low levels of education (73.94%) compared to 26.06% with secondary or higher education. In more than half of the cases (52.80%), the patients came from the peri-urban area of Bangui.

Clinical, biological and therapeutic characteristics of participants

The proportion of those with good knowledge of the clinical signs and transmission mode of the disease was relatively low, respectively 22.53% and 27.22%. According to the mode of access to healthcare at the onset of the first symptoms, the majority of the patients had sought care in informal structures 81.70% versus 18.30% for the formal structures. Regarding the choice of treatment, patients resorted to informal medicines (68.03%), traditional medicine (6.40%) and modern medicine (25.57%) at the onset of symptoms.

Table 1: Analysis of socio-demographic characteristics by time to diagnosis.

Characteristics	Delayed diagnosis					
	Short delay N (%)	Long delay N (%)	OR (95% CI)	P value	OR adjusted (95% CI)	P adjusted
Age (years)						
<35	34 (45.33)	41 (54.67)	1.22 (0.63-2.39)	0.545	-	-
>35	27 (40.30)	40 (59.70)	1			
Sex						
Male	31 (36.05)	55 (63.95)	0.48 (0.24-0.96)	0.039	0.42 (0.19-0.93)	0.03
Female	30 (53.57)	26 (46.43)	1		1	
Educational level						
None/primary	50 (47.62)	55 (53.38)	0.76 (0.56-1.06)	0.06	-	-
Secondary and plus	23 (62.16)	14 (37.84)	1			
Income level						
Acceptable	49 (66.22)	25 (33.72)	3.75 (2.18-6.43)	<0.001	2.17 (0.89-5.28)	0.09
Low	12 (17.65)	56 (82.35)	1		1	
Residence						
Urban	52 (77.61)	15 (22.39)	6.47 (3.45-12.09)	<0.001	4.35 (2.10-9.02)	0.0003
Peri-urban	9 (12.00)	66 (88.00)	1		1	

The clinical symptoms presented by the patients were classical signs of tuberculosis: cough and weight loss were reported in 95.77% of cases respectively, followed by fever (87.32%) and chest pain (85.92%). Regarding the delay in diagnosis and treatment, patients who did not receive a sputum acid-fast bacilli (AFB) test at the first consultation represented 33.10%. However, patients received their treatment on the first day of diagnosis in 81.69%. The delay of patient consultation >30 days and the diagnostic delay >30 days were observed in 83.10% and 23.94% of cases respectively.

Associated factors for delayed diagnosis

In bivariate analysis, sociodemographic factors: male gender [OR=0.48 (0.24-0.96), p=0.039]; patients from low-income households [OR=3.75 (2.18-6.43), p<0.001]; patients residing in peri-urban areas [OR=6.47 (3.45-12.09), p<0.001] (Table 1) and behavioral factors: use of informal care facilities first option [OR=2.50 (1.86-3.38), p<0.001] and not requesting AFB at first visit [OR=0.12 (0.06-0.26), p<0.001], were associated with risk of delayed diagnosis (Table 2). However, age and education level were not statistically significantly related to delay in consultation (p>0.05) (Table 2). Similarly, with regard to behavioral characteristics, there was an absence of association between patients' knowledge of the disease; clinical and paraclinical characteristics and delay in diagnosis (p>0.05) (Table 2).

In multivariate analysis, male patients [OR=0.42 (0.19-0.93), p=0.03]; patients residing in peri-urban areas (adjusted OR=4.25 (2.10-9.02), p=0.001]; patients using informal facilities as a first option [adjusted OR=1.84 (1.47-3.38), p<0.0001] and not requesting AFB at the first visit [adjusted OR=0.59 (0.48-0.75), p=0.0001] were associated with the risk of delayed diagnosis. Indeed, male patients, patients living in peri-urban areas, patients who used informal structures as a first option, and those who did not request an AFB test at the first consultation were respectively 2 times, 5 times, 2 times, and 6 times more likely to have a delay in their consultation than others (Table 2).

Table 2: Analysis behavioral characteristics of patient by delay in diagnosis.

Characteristics	Modalities	Delayed diagnosis					
		Short delay N (%)	Long delay N (%)	OR (95% CI)	P value	OR adjusted (95% CI)	P adjusted
Knowledge on TB							
No cost for diagnosis	Yes	45 (43.27)	59 (56.73)	1.05 (0.49-2.22)	0.453	-	-
	No	16 (42.11)	22 (57.89)	-			
No cost for treatment	Yes	48 (42.11)	66 (57.89)	0.84 (0.36-1.93)	0.341	-	-
	No	13 (46.43)	15 (53.57)	-			
TB symptoms	Yes	16 (50.00)	16 (50.00)	1.44 (0.66-3.18)	0.185	-	-
	No	45 (40.91)	65 (59.09)	-			
Mode of transmission	Yes	27 (45.76)	32 (54.24)	1.22 (0.62-2.38)	0.287	-	-
	No	34 (40.96)	49 (59.04)	-			
Primary care facility choice							
Structures	Formal	23 (82.14)	06 (17.86)	7.57 (2.84-20.95)	<0.001	1.84 (1.47-3.38)	<0.001
	Informal	38 (33.63)	75 (66.37)	-			
Clinic and paraclinic characteristics							
Hemoptysis	Yes	11 (31.43)	24 (68.57)	0.52 (0.23-1.17)	0.058	-	-
	No	50 (46.73)	57 (53.27)	-			
Cough	Yes	27 (51.92)	25 (48.08)	1.77 (0.89-3.55)	0.053	-	-
	No	34 (37.78)	56 (62.22)	-			
Fever	Yes	18 (52.94)	16 (47.06)	1.70 (0.78-3.69)	0.093	-	-
	No	43 (39.81)	65 (60.19)	-			
AFB request	Yes	19 (22.89)	64 (77.11)	0.12 (0.06-0.26)	<0.001	0.59 (0.48-0.75)	<0.001
	No	42 (71.19)	17 (28.81)	-			

DISCUSSION

This study highlights the different factors associated with the delay between the onset of symptoms and the time of diagnosis and treatment of TPB+.

The most affected age group in our series was 16-36 years with 69.72% of cases. This result is similar compared to those found in studies in Ethiopia in 2012 and Morocco in 2014 with 69.0% and 66.7% respectively.[4,8]

In central Africa, the prevalence of HIV/TB co-infection is very high (44%) and patients with HIV infection are increasingly young.[1,9] The male sex predominated with 60.56% of cases with a sex ratio of 1.53. This result corroborates that of several authors who have highlighted a predominance of the male sex.[1,8,10,11] According to the latest WHO report on the disease, tuberculosis affects more men than women.[3]

The proportion of persons who were unaware of the mode of transmission and signs of tuberculosis was high with 77.46% and 58.45% of cases respectively. Our results are similar to those reported by the work of Boubacar et al in

2013 in Mali and by Fentabil et al in 2017 in Ethiopia who found respectively 89.5% and 76.5%; 86.4% and 84.6% of cases.[12,13] However, Camara in Guinea did not find an association between the level of knowledge about the disease and the delay in diagnosis of TB as in our study.[14] These results could be explained by the lack of communication and awareness about TB in poor communities that are often obscured by national programs in our context.[12,15,16] However, the conclusions of several studies plead for the permanent availability of comprehensive information on the symptoms of TB and on the availability of TB services to the population. The use of these services within a reasonable time frame depends to a large extent on the patients' knowledge of the disease.[17,18]

In opposition to other common infectious diseases, diagnosis and treatment services for TB, HIV and malaria are free of charge in the Central African Republic thanks to funding from the global fund to fight the three diseases.[9] Awareness raising and education of the population would aim at changing behaviors in favor of early diagnosis of tuberculosis in order to ensure proper management. In addition, it has been noted that at the beginning of the disease, because of the triviality of the symptoms of the disease, particularly coughing, patients do not always consult a modern health service.

Among all our patients, 125 patients (88.03%) resorted to street medication at the onset of symptoms. This rate is higher than those obtained in several studies which showed that patients resorted to self-medication in 37 to 56% of cases.[4,6,19,20] The main reasons for this high proportion of choice of street drugs in our series have not been documented in the present study. A qualitative survey should be considered to better identify the reasons for this choice.

Regarding clinical symptoms, apart from hemoptysis, which was found in 21.10% of cases, the majority of our patients reported signs suggestive of tuberculosis impregnation (78.90%). The presence of these symptoms usually indicates an advanced stage of the disease.[21] This suggests that the majority of our patients would consult at an advanced stage of the disease. Several authors reported similar results.[4,16,19,20,22]

Patients with a long diagnostic delay >30 days were the least represented, representing 11.27% of cases. This result corroborates those observed by Türkkan et al in Turkey and Ravahatra et al in Madagascar.[10,12,20] On the other hand, it is higher than that observed by Chérif et al which was 26 days.[23] This high rate of diagnosis (88.73%) in less than 30 days in our series could be explained in part by the free testing for AFB in all CDTs.[9] However, the patient delay >30 days was 57.04% of cases. This same observation is observed in some studies which found a delay of more than 30 days.[8,24] However, others found a delay of less than 30 days.[6] Tuberculosis is an insidious disease with a chronic evolution. It suffers from a delay in diagnosis due to the non-specificity of the clinical signs.[25] The majority of patients generally perceive their disease as not serious and have a trivial cough that is often overlooked.[17,20,23] Moreover, patients with a long total delay >60 days in our study were the most represented, representing 46.48% of cases. This result is similar to those observed by other authors who found that almost the same proportion of patients waited more than 60 days.[4,8,23] A long delay in consultation generally lengthens the total delay.[4,6,9]

In bivariate analysis, our results showed that there was no significant association between age and delay in consultation. This same finding was found in Uganda, Senegal and Madagascar.[6,20,25] However, in Morocco, patients aged 35 years and older are less likely to have a delay in diagnosis and treatment.[4] Our study found no statistically significant relationship between clinical signs and delay in diagnosis. This finding is similar to that in Uganda.[25] In Madagascar, hemoptysis, dyspnea and asthenia were associated with delayed diagnosis.[20]

In multivariate analysis, the study showed a significant association between male gender and delayed diagnosis ($p<0.05$). Male patients in our study were 2 times more likely to have a delay in consultation compared to others ($p<0.05$). An author in Senegal found 2.5 times the risk of delayed consultation in men.[6] However, our result differs from that of several other authors, who did not find any association between gender and delay in consultation.[20,25] In our context, this finding can be explained by the fact that men generally consult late because of their lack of time, due either to their work or their activity. However, women regularly attend health facilities and are likely to come to the consultation as soon as the first signs such as coughing appear.[25]

Patients from the peri-urban areas of Bangui were 2 more likely to have a delayed diagnosis. These patients were predominant (52.80%) and almost one patient out of two (47.90%) had low income. These observations are comparable to those reported by several authors.[3,15,16] Tuberculosis is a disease closely linked to poverty, and economic difficulty is the lot of people affected by this disease.[3]

Similarly, we found a significant association between poor care pathway and delayed diagnosis ($p<0.05$). Patients who resorted to self-medication were 2.5 times more likely to have a delay in consultation than those whose first recourse was a formal structure. The same findings have been reported in a meta-analysis and other studies in Senegal and Ethiopia.[6,8,13,14]

Finally, we found a significant association between AFB request at the first visit and delayed diagnosis ($p<0.05$). Patients who did not receive AFB request at the first visit represented 33.10% of cases. They had 6 times the risk of delayed diagnosis. This finding is similar to that of several authors who found that not requesting an AFB test

was a factor related to delayed diagnosis.[6,25] This could be explained by the insufficient quality and quantity of medical personnel in the CDTs. In our health centers, most of the staff in the context of limited resources are qualified nurses, health assistants and sometimes community health workers who are less equipped to carry out a normal diagnostic process.[1,9,17]

However, this study has limitations. First, patients were recruited only from urban and peri-urban areas of Bangui, so the results cannot be extrapolated to the entire country. Second, the information about the facts of health care seeking behavior and diagnosis is self-reported, which implies some memory bias. And finally, our results certainly showed that the main factors associated with delayed diagnosis of BPT+ were: male gender, patients from a low-income household, patients residing in peri-urban areas, choosing the incorrect first-line care route, and not requesting AFB at the first consultation. A qualitative survey might have been conducted to provide more detailed information on the motivations, reasoning, and attitudes of the respondents.

CONCLUSION

This study showed that the main factors associated with delayed diagnosis of BPT+ were male gender, patients from low-income households, patients residing in peri-urban areas, poor first referral route to care, and non-request for AFB at the first consultation. In a context of high incidence of TB, coupled with a high prevalence of HIV, the diagnosis and treatment of BPT+, which is a contaminating form of the disease, emphasis should be placed on supervision and coaching of health workers coupled with increased awareness of the population on TB will contribute to better control of the disease.

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