

## *Active Search for Cases of HIV-TB co-Infection and Factors Associated with Adherence to Treatment in Co-Infected Patients in the City of Douala*

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### **ABSTRACT**

**Introduction:** Human Immunodeficiency Virus (HIV)-tuberculosis (TB) co-infection is among the major determinants of infectious morbidity and mortality in the developing world. Limited access to effective, quality-assured health services for these transmissible diseases among the poor is a major obstacle to achieving the Sustainable Development Goals for health. Late detection of TB/HIV co-infection is the leading cause of death among co-infected patients. Of an estimated 10.4 million new cases, only 6.1 million were detected and reported in 2015. The objective of this study was to analyze the factors associated with adherence to treatment of HIV-TB co-infected patients identified through an active search process in the city of Douala.

**Materials and Methods:** From April 2019 to January 2020, we conducted a two-stage observational study. In the first phase, we sought out HIV-TB co-infected patients and in the second phase, we followed up on these cases in formal and informal health facilities in the city of Douala. 42 patients participated in the study, the majority (83%) of whom were from formal health facilities. Clinical diagnoses were made based on the case definition and after that, biological tests were done for the confirmation of Microscopy Positive Pulmonary Tuberculosis (MPTP) in patients to be included in the treatment. Screened cases were submitted to a questionnaire and then followed up during the treatment period. The data collected were analyzed using SPSS version 22.0 and Microsoft Excel 2016.

**Results:** During the collection period we had 07 cases of TB/HIV co-infection in the informal health facilities that were referred to TB Control Centers. We had 35 cases in the formal health facilities. Of the 07 HIV-TB co-infected patients in the informal health facilities, 71.4% were between the age group 31 to 40 years. Factors linked to patients (social, psychological, and knowledge of infection factors, perception of the disease and treatment) and factors linked to treatment (simplicity of treatment and interruption in treatment) did not influence adherence to treatment. The association between these factors is not statistically significant at the 5% significance level. With a p-value of 0.001 regarding factors linked to the therapeutic environment, only the reason for consulting the health facility influences adherence to treatment by the patients surveyed. Thus, the association between the reasons for consultation in the health facility and adherence to treatment is statistically significant at the 5% significance level.

**Conclusion:** The main results show that most patients from both formal and informal health facilities adhered to the different treatments. There was no difference in treatment adherence between the two groups.

**Keywords:** Adherence, Anti-tuberculosis Treatment, Anti-retroviral Therapy, Patient, Co-Infection TB/VIH.

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**Crossref Doi:** <https://doi.org/10.36437/irmhs.2023.6.2.D>

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**Introduction**

Tuberculosis is truly one of the leading killers of people living with the Human Immunodeficiency Virus.<sup>1</sup> At least one in four deaths among people living with HIV is attributed to TB, and many of these deaths occur in resource-limited countries. Despite efforts to improve community TB case detection and reduce TB incidence, TB case detection rates remain below the global target of at least 70%.<sup>2</sup>

Timely access to TB services is complicated by both patient, treatment, and therapeutic environment barriers, such as reception conditions, proximity to the health facility, the carer patient relationship, free care, good coordination of TB and HIV services, drug supply management and possible anticipation of setbacks, which in turn increases patient drop-out during care-seeking.<sup>3</sup> Collaboration for TB and HIV activities is essential to prevent, diagnose and treat TB in patients living with HIV and HIV in TB patients, to ensure that TB patients living with HIV are identified and treated correctly. In the area of prevention of TB in people living with HIV, the top research priorities are an optimal TB screening algorithm that can be used in settings with varying prevalence of TB and HIV, to safely initiate TB preventive treatment; the best infection control interventions that effectively reduce transmission of Mycobacterium tuberculosis in communities. In the area of intensified TB case-finding, the development of innovative strategies that are simple, rapid, and usable in the community has been recognized as the top priority.<sup>4</sup>

This study falls within the field of public health and, more specifically, the epidemiology of TB/HIV co-infection. Late detection of TB/HIV co-infection is the main cause of death in co-infected patients. The global rate of reduction in

tuberculosis cases remained at 1.5% between 2014 and 2015 and must rise to 4-5% by 2020 if the first milestone in the World Health Organization (WHO) Strategy to Stop TB is to be reached. An estimated 4.3 million cases of tuberculosis remain undetected [2]: this is a public health problem and countries must therefore focus on the prevention, detection and treatment of tuberculosis in order to achieve the targets set in the WHO strategy.<sup>1,5</sup>

Given that tuberculosis is much more prevalent in low-income populations using informal care providers, it is important to place particular emphasis on the rapid detection of new cases, as the immune deficiency associated with HIV infection favors the transition from latent tuberculosis to active tuberculosis. The burden of tuberculosis in Africa, and particularly in Cameroon, is exacerbated by HIV infection. While HIV infection weakens patients' immune systems and makes them susceptible to TB, this in turn encourages replication of the virus<sup>6</sup>, creating a vicious circle. The strategies adopted in Cameroon by the National Tuberculosis Control Program (NTCP) are to take a comprehensive approach to all aspects of the fight against tuberculosis, as recommended by the WHO. In order to speed up the provision of Anti-Retroviral Therapy (ART) for People Living with HIV/AIDS (PLHIV), the country has undertaken to improve the geographical and financial accessibility of treatment services throughout the country.<sup>7</sup>

**Materials and Methods**

This is an observational study which took place in two stages, over a 10-month period from April 2019 to January 2020.



addition, information on co-infected patients was recorded according to the various informal health facilities. After checking the conformity of each survey form, the information collected was stored in the Census Survey Processing (CSPPro) software using a specially designed input mask. The data was then checked, transferred, and analyzed using Statistical Package Social Sciences (SPSS).

**Ethical Considerations**

We obtained ethical approval (N°2020/020146/CEIRSH/ESS/MSP) from the Institutional Ethics Committee of Research for Human Health (CEIRSH), the Ministry of Public Health (N° 30-327/MINSANTE/SG/DROS), the regional delegation of the Ministry of Public

Health and the administrative authorities of the various Health Facilities. The anonymity and confidentiality of the information gathered were ensured, as was respect for the rights and freedoms of the participants.

**Results**

**Factors linked to patients**

In total, among patients referred to the TB Treatment Centers, we had 07 cases of TB/HIV co-infection out of the 23 patients who tested positive for TB in the informal health facilities. This gives us a prevalence of about 30.4%. Of the 07 TB/HIV co-infected patients from informal health facilities, 71.4% were in the 31-40 age group.

Characteristics		Informal (N=7)		Formal (N=35)		Total (N=42)	
		n	%	N	%	n	%
Sex	Male	4	57,1	10	28,5	14	33,3
	Female	3	42,9	25	71,5	28	66,7
Average age (ET)		35,14(8,63)		38,71(10,68)		38,12(10,36)	
Age							
	18-30	1	14,3	11	31,4	12	28,6
	31-40	5	71,4	8	22,9	13	31
	41-50	0	0	10	28,6	10	23,8
	51-60	1	14,3	6	17,1	7	16,6
Marital status							
	Married	6	85,7	14	40	20	47,6
	Single	1	14,3	17	48,6	18	42,9
	Divorced	0	0	1	2,8	1	2,4
	Widowed	0	0	3	8,6	3	7,1

**Table 1: Socio-demographic characteristics of patients surveyed.**

The predominant sex among co-infected patients from informal health facilities is male (57.1%), whereas, in formal health facilities, it is female, with a participation rate of 71.5%. The table shows that in the informal health facilities, 71.4% of patients were aged between 31 and 40. There were no patients aged between 41 and 50. The average age of these patients was 35.14. In formal health facilities, the table shows that 31.1% of

patients were aged between 18 and 30. The average age of patients was 38.71. The youngest patient was 19 and the oldest was 59. In the informal category, there were only two categories of patients' marital status. 85.5% of patients were married and only 14.3% were single. In the formal sector, 48.6% of patients surveyed were single, while only 2.8% were divorced (Table 1).

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)	
	N	%	n	%	n	%
<b>School level</b>						
None	0	0	3	8,6	3	7,2
Primary	2	28,6	8	22,8	10	23,8
Secondary	4	57,1	21	60	25	59,5
Higher	1	14,3	3	8,6	4	9,5
<b>(Méd; q1, q3)</b>	2; 1; 4		2; 1; 4		2; 1; 4	
<b>Number of children</b>						
0-2	4	57,1	21	60	25	59,5
3- 4	2	28,6	10	28,6	12	28,6
5- 6	1	14,3	4	11,4	5	11,9
<b>Religion</b>						
Catholic	3	42,8	13	37,1	16	38,1
Protestant	2	28,6	13	37,1	15	35,7
Muslim	2	28,6	3	8,6	5	11,9
Secular	0	0	4	11,5	4	9,5
Other	0	0	2	5,7	2	4,8
<b>Profession</b>						
Civil servant	1	14,3	6	17,1	7	16,6
Unemployed	2	28,6	8	22,8	10	23,8
Student	0	0	1	2,9	1	2,4
Student (Higherschool)	1	14,3	1	2,9	2	4,8
Shopkeeper/Farmer	3	42,8	19	54,3	22	52,4

**Table 2: Socio-demographic characteristics of patients surveyed.**

Table 2 shows that for informal patients, almost five out of seven have at least secondary education, with secondary education dominating, accounting for 57.1% of patients. For formal patients, over 90% are educated, with secondary education dominating (60%). In the informal sector, the predominant religion is Catholic (42.8%) and the other two religions (Protestant

and Muslim) share the same score of 28.6% respectively. In the formal sector, the predominant religions are Catholic and Protestant respectively, with a percentage of 37.1% each, and only 5.7% belong to other religions. The dominant types of patients are shopkeepers/farmers (52.4%), the unemployed (23.8%), and civil servants (16.6%).

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)		P-Value
	n	%	N	%	n	%	
<b>Taking ART</b>							-
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	

<b>Reason for taking ART</b>							0,638
To protect Partner	1	14,3	3	8,6	4	9,5	
To improve health	6	85,7	32	91,4	38	90,5	
Motivation of family and friends	0	0	0	0	0	0	

\*\*\* significant at 1%; \*\* significant at 5 %; \* significant at 10%.

**Table 3: Breakdown of patients' psychological factors.**

Table 3 shows that the psychological factors of the patients surveyed do not influence adherence to

treatment. The association is not statistically significant at the 5% significance level.

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)		P-Value
	N	%	N	%	n	%	
<b>Opinion on illnesses</b>							0,654
Mystical illnesses	0	0	2	5,7	2	4,8	
Diseases like any other	6	85,7	28	80	34	81	
Shameful illnesses	1	14,3	2	5,7	3	7,1	
Others	0	0	3	8,6	3	7,1	
<b>Can tuberculosis be treated?</b>							--
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	
<b>Personal feelings</b>							0,751
Guilty	3	42,9	13	37,1	16	38,1	
Outcast	0	0	3	8,6	3	7,1	
No feeling	3	42,9	10	28,6	13	31	
Others	1	14,2	8	22,9	9	21,4	
<b>Treatment can improve health</b>							--
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	

\*\*\* significant at 1%; \*\* significant at 5 %; \* significant at 10%.

**Table 4: Relationship between informal and formal patients' understanding and perception of the disease and treatment.**

Table 4 shows that, at the 5% significance level, the association between understanding and perception of the disease and the treatment of the

patients surveyed does not influence adherence to treatment among patients in formal and informal health facilities.

**Factors linked to treatment**

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)		P-Value
	N	%	n	%	n	n	%
<b>Difficulty taking medication</b>							<b>0,067*</b>
Yes	4	57,1	8	22,9	12	28,6	
No	3	42,9	27	77,1	30	71,4	
<b>Frequency of taking medication</b>							0,651
Unbearable	0	0	8	22,9	1	2,4	
Bearable	7	100	27	77,1	41	97,6	
Others	0	0	0	0	0	0	
<b>Reason for difficulty in taking medication</b>							0,303
Multi-Daily doses	0	0	0	0	0	0	
Untolerated side effects	1	14,3	4	11,4	5	11,9	
Time constraints	3	42,9	3	8,6	6	14,3	
Taste of the drug	0	0	0	0	0	0	
Fear of stigma	0	0	0	0	0	0	
Others	0	0	0	0	0	0	

\*\*\* significant at 1%; \*\* significant at 5 %; \* significant at 10%.

**Table 5: Breakdown of factors linked to patients' simplicity of treatment and discontinuation of treatment.**

A factual analysis of this table shows that there is no statistically significant association at the 5% significance level between the simplicity of

treatment, discontinuation of treatment by patients surveyed, and adherence to treatment (Table 5).

**Factors linked to the therapeutic environment**

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)		P-Value
	n	%	n	%	n	N	%
<b>Reason for consultation in the health facility</b>							<b>0,001***</b>
Saves time	4	57,1	0	0	4	9,5	
Less cumbersome procedures	0	0	2	5,7	2	4,8	
Confidentiality	3	42,9	12	34,3	15	35,7	
Better care	0	0	13	37,1	13	31	
Free	0	0	3	8,6	3	7,1	
Confidence in staff	0	0	2	5,7	2	4,8	
Proximity	0	0	3	8,6	3	7,1	
<b>Have you heard about TB Treatment Center?</b>							0,517

Yes	6	85,7	26	74,3	32	76,2	
No	1	14,3	9	25,7	10	23,8	
<b>Reception at the TB Treatment Center</b>							0,109
Not good	0	0	0	0	0	0	
Good	6	85,7	18	51,4	24	57,1	
Very good	1	14,3	16	45,7	17	40,5	
<b>Explanation of treatment</b>							--
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	
<b>Information provided</b>							0,359
Not understandable	0	0	0	0	0	0	
Understandable	6	85,7	24	68,6	30	71,4	
Quite understandable	1	14,3	11	31,4	12	28,6	

\*\*\* significant at 1%; \*\* significant at 5 %; \* significant at 10%.

**Table 6: Breakdown of factors relating to patients' therapeutic environment.**

Characteristics	Informal (N=7)		Formal (N=35)		Total (N=42)		P-Value
	N	%	n	%	N	%	
<b>Satisfied with explanations given by medical staff</b>							--
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	
<b>Would you recommend TB Treatment &amp; ART Centers?</b>							--
Yes	7	100	35	100	42	100	
No	0	0	0	0	0	0	
<b>Areas for improvement</b>							0,541
Reception	0	0	9	25,7	9	21,4	
Long waiting times	4	57,1	18	51,4	22	52,4	
Attention of healthcare providers	0	0	1	2,9	1	2,4	
Lack of comprehensive information	0	0	0	0	0	0	
Others	1	14,3	4	11,4	5	11,9	

\*\*\* significant at 1%; \*\* significant at 5 %; \* significant at 10%.

**Table 7: Breakdown of factors relating to patients' therapeutic environment.**

It is clear from this table that, as regards factors linked to the therapeutic environment, only the reason for consulting the health facility had an influence on adherence to treatment among the patients surveyed. The association is statistically significant at the 5% significance level. (Table 7)

### **Discussion**

The study of adherence to anti-tuberculosis treatment and antiretroviral therapy among TB/HIV co-infected patients in formal and informal health facilities in the city of Douala suggests the possibility of integrating informal health facilities into the various TB and HIV control programs. The aim would be to optimize the screening of TB/HIV co-infected patients, thereby reducing the mortality rate from these diseases due to late screening in Cameroon. Factors linked to patients, treatments, and the therapeutic environment will be discussed.

### **Factors linked to patients**

Factors linked to patients include social factors, psychological factors, understanding and perception of the disease, and treatment. Regarding social factors, it emerged that patients from formal and informal health facilities share the same characteristics. These factors found in both types of patients did not influence their adherence to treatment. Here we can explain this phenomenon by the fact that we chose to work only with patients who were at least 18 years old, which implies that we were dealing with adult patients who had reached the age of majority. Patients with these characteristics adhere well to the various treatments. This would be in line with the conclusions of Issoufi<sup>8</sup>, Stone, et al.<sup>9</sup>, for whom patients aged under 50 are the most adherent. Of the 07 cases found in the informal health facilities, 05 were men, which could be explained by the fact that most of the time men avoid public hospitals because they always want to be served quickly.<sup>10,11</sup> The sex ratio was 0.75 in informal health facilities and 0.4 in formal health facilities.

Psychological factors include feelings of discouragement. In this study we found that 100%

of the patients surveyed replied that they were taking their ART. As for the reason for taking ART, we found that 85.7% of patients from health facilities and 91.4% of patients from formal health facilities said they were taking the treatment to improve their health. These two values show that these two categories of patients have the same reasons for taking medication. This can be explained by the fact that when patients know that a treatment can improve their health, they are more motivated to follow the treatment through to the end. As the Health Belief Model theory states, patients' awareness of their illness and their interest in their treatment have an impact on compliance.<sup>12</sup> In this respect, we need to consider the value that patients co-infected with TB/HIV place on their survival and their desire to get better despite their seropositivity. According to the health belief model, the adoption of a behavior depends on the seriousness of the problem, the perception of risk, the benefits of the behavior to be undertaken, the perception of obstacles, and the belief in one's own efficacy. Patients are more likely to adopt a new behavior if they believe they can do it.

The understanding and perception of the disease and treatment are the same among patients in formal and informal health facilities. This could be explained by the fact that once in the treatment centers, all these patients received the same explanations about the disease. In our study, the association between the understanding, perception of the disease, and treatment of the patients surveyed did not influence adherence to treatment among patients in the formal and informal sectors.

### **Factors linked to treatment**

Factors linked to treatment refer to the simplicity of treatment and the interruption of treatment. We found that 57.1% of patients from informal health facilities said they had difficulty taking their medication, whereas 77.1% of patients from formal health facilities said they had no difficulty taking their medication. The association of this

factor with adherence to treatment is significant at the 10% level. This result, although not significant at the 5% threshold that was set at the start of this study, shows convergence with the literature, since simplicity of treatment improves adherence to treatment.<sup>13</sup> The use of fixed doses simplifies treatment by reducing the number of tablets and prevents patients from taking only part of the treatment prescribed.<sup>14,15</sup> On average, the majority of patients surveyed found the frequency with which they took their medication tolerable. As for the reason for the difficulty in taking medicines, 57.1% of patients from informal health facilities mentioned adverse effects that they could not tolerate, while 88.6% of patients from formal health facilities mentioned time constraints. This is in line with the literature. Patients often interrupt their treatment because of side effects, so it is essential to detect them and treat them quickly. For drug-resistant TB patients, day-to-day support is necessary because of the large number of tablets to be taken each day.

#### **Factors linked to the therapeutic environment**

These factors are linked to the reception conditions in the treatment centers, the proximity of the health facility, the relationship between the carer and the patient, the fact that care is free, the good coordination of TB and HIV care services, the management of drug supplies and the anticipation of possible setbacks. It is clear from our analyses that the reason for consultation at the health facility influences adherence to treatment among the patients surveyed ( $P=0.001$ ).<sup>16-18</sup> 57.1% of patients from the informal sector chose time-saving as the reason for going to the informal health facility, whereas most patients from the formal health facility (37.1%) gave better care as the reason for going to the formal health facility.

These findings suggest that there is an interest in actively seeking out cases of co-infection in the community, and more specifically in informal health facilities. Referral of patients from informal health facilities to diagnostic and treatment centers can be done without restraint, without

worry, and lead to equality in care with patients from formal health facilities.

#### **Conclusion**

This study showed that most patients from formal and informal health facilities adhered to the various anti-tuberculosis treatments and antiretroviral therapy. Adherence to treatment is influenced only by the therapeutic environment. She worked to gradually encourage decision-makers to set up a platform for systematic referral of suspected cases from informal health facilities to formal health facilities. There is an interest in actively seeking out cases of co-infection in the community, and more specifically in informal health facilities. Referral of patients from informal health facilities to diagnostic and treatment centers can be carried out without restraint or concern, leading to equality of care with patients from formal health facilities.

#### **Contribution of authors**

Onana A. F. Anicet, and Sylvie K. Nolna, designed the study. Onana A. F. Anicet collected the data and wrote the manuscript. Ndibi A. Jean, Tchoffo Désiré, and Pearl N. Mbu reviewed the manuscript, and Sylvie K. Nolna supervised the work. Tchinda F. Cedric made a critical reading of the manuscript. All authors have given their approval for publication.

#### **Acknowledgements**

The author addresses their sincere gratefulness to the National Tuberculosis Control Programme (NTCP) for their support and for facilitating access to the data collection process.

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**How to cite this Article:** Onana Akoa François Anicet, Ndibi Abanda Jean, Tchoffo Désiré, Tchinda Fossi Cedric, Pearl Nsom Mbu, Sylvie Kwedi Nolna; [Active Search for Cases of HIV-TB co-Infection and Factors Associated with Adherence to Treatment in Co-Infected Patients in the City of Douala](#); *Int. Res. Med. Health Sci.*, 2023; (6-2): 22-33; doi: <https://doi.org/10.36437/irmhs.2023.6.2.D>

**Source of Support:** Nil, **Conflict of Interest:** None declared.

**Received:** 15-03-2023; **Revision:** 10-05-2023; **Accepted:** 27-05-2023