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Factors of Adherence to Concurrent Tuberculosis Treatment and Antiretroviral Therapy among HIV-TB Co-Infected Individuals in the East Region, Cameroon in the COVID-19 Era: A Retrospective Cohort Study

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Abstract

Context/Objectives: Tuberculosis (TB) and HIV co-infection is a serious health problem in Cameroon. The problems associated with poor adherence to treatment are on the increase worldwide. This problem can be observed in all situations where patients are required to administer their own medication, whatever the type of illness. The general objective of this study was to assess the factors affecting adherence to treatment among HIV-TB co-infected patients in health facilities in the East Region in the COVID context. **Method:** A retrospective cohort study before and during COVID-19 was conducted in HIV care units in 13 health districts in the East Region of Cameroon. Data were collected using a questionnaire recorded in the Kobo Collect android application, analyzed using SPSS version 25 software and plotted using Excel. **Results:** The pre-COVID-19 cohort compared to the during-COVID-19 cohort had a 1.90 risk of not adhering to treatment (OR: 1.90, CI {1.90 - 3.37}) and the difference was statistically significant at the 5% level (p-value = 0.029). Frequency of adherence was 65.4% (140/214). Adherence before COVID-19 was 56.9% whereas during COVID-19, it was 74.3%. **Conclusion:** The implementation of targeted interventions in the COVID-19 context, using evidence-based data and integrating the individual needs of HIV-TB co-infected patients, improved adherence to concurrent anti-tuberculosis treatment and antiretroviral therapy during the COVID-19 Era.

Keywords

Factors of Adherence, Tuberculosis Treatment, Antiretroviral Therapy, HIV-TB Co-Infection, East Region, Cameroon

1. Introduction

One of the complex human behaviours in which healthcare professionals and patients share responsibility for the implementation and day-to-day monitoring of a therapeutic outcome is called therapeutic adherence or adherence to treatment in the context of the optimization and success of therapeutic treatments. The WHO defines adherence as "the extent to which a person's behaviour—taking medication, following a diet and/or making lifestyle changes—corresponds to agreed recommendations from a health professional" [1].

The WHO report confirms that poor long-term adherence to treatment seriously compromises the effectiveness of therapy. This definition of adherence has evolved over time. It ranges from passive adherence by the patient of the prescribed treatment ("compliance") to active adherence ("adherence"). Allenet *et al.* (2018) [2] describe this shift in definition as moving from "the gap between what the patient does versus what the doctor says" to "the gap between what the patient does versus what the patient and doctor have decided after negotiation without imposition".

The WHO report confirms that poor long-term adherence to treatment seriously compromises the effectiveness of therapy. Indeed, as discussed in the editorial by Costedoat-Chalumeau *et al.* (2018) [3] in the special issue on treatment adherence in the journal Rheumatology, the consequences of non-adherence are well demonstrated and there is a higher risk of emergency department visits and hospitalisation in the following year, more persistent disease activity, flare-ups and unnecessary treatment escalation. Worldwide, it is estimated that the avoidable costs associated with lack of adherence to treatment exceed 470 billion dollars, or around 8% of annual healthcare expenditure [4]. Health services therefore need to pay particular attention to understanding patients' needs [5].

The COVID-19 pandemic has introduced new challenges in the management of HIV-TB co-infected patients. Understanding how these challenges affect adherence to treatment is essential to improving healthcare in this context. This pandemic has disrupted healthcare systems around the world, including those in Cameroon. Health resources and personnel have been redirected to the fight against COVID-19, which may have repercussions on the management of other diseases, including tuberculosis and HIV. The objective of this study was to assess the factors affecting adherence to treatment among HIV-TB co-infected patients in health facilities in the Eastern Region in the COVID context.

2. Methods

2.1. Study Design

We conducted a retrospective cohort study of 262 HIV-TB co-infected patients undergoing treatment in 11 health facilities within 13 health districts in the East region of Cameroon. These patients were divided into 2 cohorts, a pre-COVID-19 cohort (158 patients) and a post-COVID-19 cohort (104 patients). This longitudinal observational study was conducted over a 25-month period from April 2019 to April 2021. According to the COVID-19 status report (SITREP), the East Region of Cameroon recorded its first new case of COVID-19 on 8 April 2020. Data were collected using a questionnaire and an interview guide. The socio-economic and demographic characteristics are as follows: age, gender, matrimonial status, educational level, profession, monthly income and division. The factors related to the patients' adherence are: factors linked to the patient (monthly income, religion, residence, type of health facility visited by the patient, distance from home to health facility), factors linked to treatment (type of tuberculosis, presence of undesirable effects) and factors linked to the environment (attitude of family or relatives, help with taking medication, COVID-19). In the context of our study, we utilized the self-assessment questionnaires from the study "Self-reported adherence to antiretroviral medication among participants in HIV clinical trials: The AACTG Adherence Instruments" by Margaret Chesney. We adapted these questionnaires for our study to address our research questions. It consisted of two main sections: socio-economic and demographic factors, and factors related to the patient, treatment, and therapeutic environment. The reliability and validity of this questionnaire were tested two weeks before the survey with a group of 10 individuals, including 7 HIV-TB co-infected patients and 3 healthcare professionals.

2.2. Sampling

We used cluster sampling technique. After studying the field and taking into account the long distances separating the different health districts, we randomly selected a HIV treatment unit and all the HIV-TB co-infected patients during the periods from April to September 2019 and from May to October 2020 constituted our sample. According to the inclusion criteria, a total of 262 HIV/TB co-infected patients and aged at least 18 years accepted to participate in our study.

2.3. Statistical Methods

The questionnaire was edited in Excel and imported into Kobo Collect, then used for digital data collection on an Android phone. Data were collected during the patient's appointment at the health facility or during home visits. The socio-economic and demographic characteristics of patients co-infected with HIV-TB, as well as factors related to the patient, the treatment and the therapeutic environment in the COVID-19 context that could influence adherence to anti-tuberculosis treatment and antiretroviral therapy were collected. Data collection authorizations were obtained from the East Regional Delegation of Public Health and the various health districts involved in the study. The comparison of proportions was conducted using Pearson's Chi^2 tests. Bivariate and multivariate logistic regression (likelihood ratio) was employed to identify risk factors for adherence and explore factors associated with treatment adherence in co-infected patients. The association was expressed using Odds Ratio (OR) with a 95% confidence interval. Multivariate analysis was performed using the binomial logistic regression model. The significance threshold in our study was set at 5% for the conducted analyses. The collected data were analyzed using SPSS version 25 software, and graphs were created using Excel 2019.

3. Results

3.1. Socio-Demographic Characteristics by Cohort Type

Table 1 shows whether socio-demographic characteristics such as age, sex, marital status, level of education, occupation, monthly income, religion, division, place of residence and distance from the patient's residence to the health facility are identical in the two types of cohorts (cohort before COVID-19 and cohort during COVID-19).

Table 1 shows that sex (p-value = 0.010) and division (p-value = 0.021) were not distributed in the same way between the two types of cohorts.

3.2. Clinical Characteristics by Type of Cohort

Table 2 presents the clinical characteristics of patients by cohort type. The results show that the patient status (p-value = 0.033) of the participants is not distributed in the same way in the two types of cohorts (cohort before COVID-19 and cohort during COVID-19), whereas the other characteristics such as patient outcome, type of tuberculosis, TB treatment protocol, knowledge of duration of treatment and adverse effects are distributed in the same way between the two types of cohorts.

3.3. Family Characteristics and Habitat by Type of Cohort

Table 3 shows the family characteristics and habitat of patients by type of cohort. The results show that participants' compliance with anti-COVID-19 barrier measures (p-value = 0.006) is not distributed in the same way in the two types of cohorts (cohort before COVID-19 and cohort during COVID-19). On the other hand, other characteristics such as the attitude of the family/close friends towards the patient, assistance in taking medication and drug use were distributed in the same way between the two types of cohorts.

3.4. Level of Adherence to Treatment in Co-Infected Patients

We calculated the frequency of adherence to antiretroviral therapy and antituberculosis treatment according to the type of cohort and by division.

3.4.1. Frequency of Adherence According to Type of Cohort

As seen in Figure 1, the frequency of adherence was 65.4% (140/214). Adherence before COVID-19 was 56.9% whereas during COVID-19 it was 74.3%. This result shows that there was better adherence to treatment during COVID-19 than before COVID-19. The difference is significant at the 5% significance level.

Table 1. Socio-demographic characteristics by type of cohort.

Characteristics	Cohort			
	N (%)	Before COVID-19 (%)	During COVID-19 (%)	p-value
Age year (mean ± SD*)	39.3 ± 11.4	40.0 ± 12.4	39.7 ± 10.3	0.563
Gender				0.010
• Female	111 (51.9)	66 (60.6)	45 (42.9)	
• Male	103 (48.1)	43 (39.4)	60 (57.1)	
Matrimonial status				0.089
• Single	81 (38.2)	48 (44.0)	33 (38.2)	
• Divorce	8 (3.8)	6 (5.5)	2 (1.9)	
• Married	106 (50.0)	46 (42.2)	60 (58.3)	
• Widower	17 (8.0)	9 (8.3)	8 (7.8)	
Educational level				0.121
• None	15 (7.1)	10 (9.2)	5 (4.9)	
• Primary	95 (44.8)	55 (50.5)	40 (38.8)	
• Secondary	97 (45.8)	42 (38.5)	55 (53.4)	
• University	5 (2.4)	2 (1.8)	3 (2.9)	
Profession				0.486
• Farmer/artisan	73 (34.3)	40 (37.0)	33 (31.4)	
• Trader	69 (32.4)	30 (27.8)	39 (37.1)	
• Unemployed	45 (21.1)	23 (21.3)	22 (21.0)	
• Employed	26 (12.2)	15 (13.9)	11 (10.5)	
Monthly income				0.336
• <50,000 Fcfa	97 (46.2)	55 (50.5)	42 (41.6)	
• 50,000 - 100,000 Fcfa	95 (45.2)	44 (40.4)	51 (50.5)	
• ≥100,000 Fcfa	18 (8.6)	10 (9.2)	8 (7.9)	
Division				0.021
• Boumba et Ngoko	8 (3.7)	5 (4.9)	3 (2.7)	
• Haut Nyong	57 (26.6)	20 (19.4)	37 (33.3)	
• Kadey	11 (5.1)	9 (8.7)	2 (1.8)	
• Lom et Djerem	138 (64.5)	69 (67.0)	69 (62.2)	

*SD: Standard Deviation.

Table 2. Clinical characteristics by type of cohort.

Characteristics	Cohort			p-value
	N (%)	Before COVID-19 (%)	During COVID-19 (%)	
Patient status				0.033
• New	206 (96.3)	108 (99.1)	98 (93.3)	
• Relapse	8 (3.7)	1 (0.9)	7 (6.7)	
Patient outcome				0.171
• Interruption of treatment	9 (4.2)	7 (6.4)	2 (1.9)	
• On treatment	205 (95.8)	102 (93.6)	103 (98.1)	
Type of tuberculosis				0.539
• Extra-pulmonary	31 (15.1)	17 (16.7)	14 (13.6)	
• Pulmonary	174 (84.9)	85 (83.3)	89 (86.4)	
TB treatment protocol				1.0
• RH	4 (2.3)	2 (2.3)	2 (2.2)	
• RHEZ	171 (97.7)	84 (97.7)	87 (97.8)	
Knowledge of treatment duration				0.769
• Yes	194 (94.6)	97 (95.1)	97 (94.2)	
• No	11 (5.4)	5 (4.9)	6 (5.8)	
Side effect				0.924
• Yes	134 (65.4)	67 (65.7)	67 (65.0)	
• No	71 (34.6)	35 (34.3)	36 (35.0)	

Table 3. Family characteristics and habitat by cohort type.

Characteristics	Cohort			p-value
	N (%)	Before COVID-19 (%)	During COVID-19 (%)	
Attitude of family and friends				0.744
• Discriminatory	38 (18.5)	18 (17.6)	20 (19.4)	
• Not discriminatory	167 (81.5)	84 (82.4)	83 (80.6)	
Help with taking medication				0.916
• Yes	142 (69.3)	71 (69.6)	71 (68.9)	
• No	63 (30.7)	31 (30.4)	32 (31.1)	
Drug use				0.983
• Yes	18 (8.8)	9 (8.8)	9 (8.7)	
• No	187 (91.2)	93 (91.2)	94 (91.3)	
Compliance with anti-COVID-19 barrier measures				0.006
• Yes	38 (19.4)	26 (27.4)	12 (11.9)	
• No	158 (80.6)	69 (72.6)	89 (88.1)	

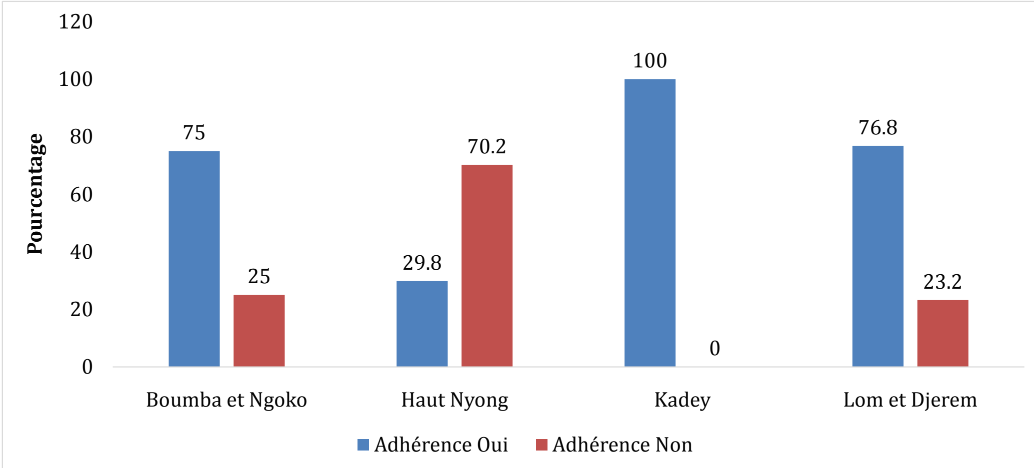

Figure 1. Adherence according to type of cohort.

3.4.2. Adherence by Divisions

Figure 2 shows that adherence to treatment in the Boumba and Ngoko division was 75%. In Haut Nyong division, adherence to treatment was 29.8%. In Kadey division, adherence to treatment was 100% and in Lom et Djerem division, 76.8%. The difference observed was statistically significant between the 4 departments (p-value < 0.001).

3.5. Factors Influencing Adherence to Concurrent TB and Antiretroviral Treatments

3.5.1. Factors Linked to Patient

The results presented in Table 4 provide valuable insights into the factors influencing adherence to TB and ART concurrent treatment. The statistical analysis revealed significant associations between adherence and several demographic and contextual variables. Religion emerged as a significant factor influencing adherence ($p < 0.001$). Lay individuals showed a substantial 6.94-fold risk of non-adherence compared to Christians, signifying a noteworthy risk. However, the risk among Muslims was not statistically significant.

Residence type was found to be a significant factor ($p = 0.008$), with patients in rural areas facing a 2.20-fold risk of non-adherence compared to their urban counterparts. This suggests that living in a rural area is a notable risk factor for poorer adherence.

The type of health facility was strongly associated with adherence ($p < 0.001$). Patients attending public health facilities exhibited a striking 19.93-fold risk of non-adherence compared to those in private health facilities. This highlights a substantial risk linked to receiving treatment in public health facilities.

The distance of residence from the health facility was also a significant factor ($p = 0.012$). Individuals residing more than 10 km away from the health facility faced a 2.09-fold risk of non-adherence compared to those living within a 10 km radius. This underscores the impact of distance as a risk factor for adherence.

Residing more than 10 km from the health facility, living in a rural area, seeking treatment in a public health facility, and being a lay person were identified as risk factors associated with poor adherence to concurrent TB and ART treatment. These findings provide crucial information for healthcare providers and policymakers to develop targeted interventions and support strategies tailored to these specific risk factors, ultimately enhancing treatment adherence among co-infected individuals.

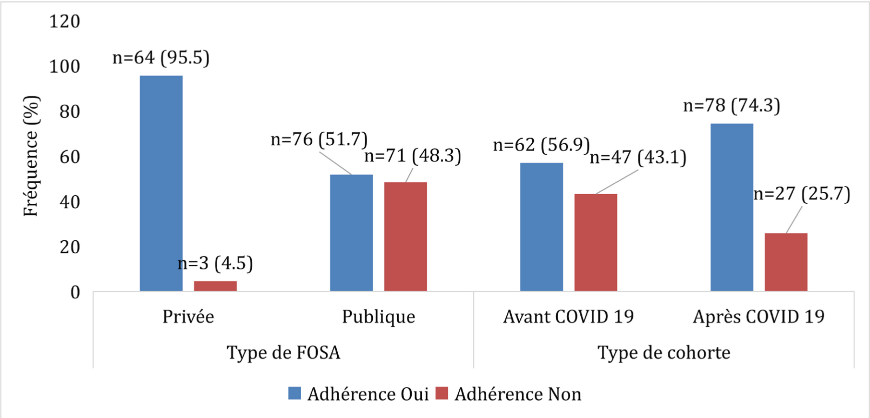

Figure 2. Adherence by divisions.

Table 4. Socio-demographic characteristics (Bivariate).

Characteristics	Adherence (%)	OR	CI at 95%	p-value
Monthly income				0.118
• <50,000 Fcfa	68 (70.1)	1	-	
• 50,000 - 100,000 Fcfa	61 (64.2)	1.31	0.71 - 2.39	
• ≥100,000 Fcfa	8 (44.4)	2.93	1.05 - 8.18	
Religion				<0.001
• Christian	111 (69.8)	1	-	
• Lay	6 (25.0)	6.94	2.59 - 18 - 56	
• Muslim	19 (76.0)	0.73	0.27 - 1.94	
Residence				0.008
• Rural	66 (57.4)	2.20	1.22 - 3.94	
• Urban	74 (74.7)	1	-	
Type of health facility				<0.001
• Private	64 (95.5)	1	-	
• Public	76 (51.7)	19.93	5.99 - 66.31	
Distance from home to health facility				0.012
• Less than 10 Km	86 (72.9)	1	-	
• More than 10 Km	54 (56.3)	2.09	1.18 - 3.70	

3.5.2. Factors Linked to Treatment

The results in Table 5 show that the type of tuberculosis (p = 0.317) and knowledge of the duration of treatment (p = 0.509) were not risk factors (p > 0.05). However, the follow-up cohort (p = 0.029) and adverse events (p < 0.001) were risk factors. For the cohort followed before COVID-19, compared with the cohort followed during COVID-19, there was a 1.90 risk of not adhering to treatment. This indicates a notable difference rate between the two cohorts, with the cohort before COVID-19 facing a higher risk of non-adherence.

3.5.3. Factors Linked to Environment

The results in Table 6 show that drug use (p = 0.442) and compliance with anti-COVID-19 barrier measures (p = 0.114) were not risk factors (p > 0.05). However, the attitude of family and friends (p = 0.008) and assistance in taking medication (p = 0.010) were risk factors. Patients who live in an environment where there is a discriminatory attitude towards them due to their double burden have a 2.66 risk of not adhering to treatment compared with patients who do not experience any discrimination from their environment (family, close relations). Patients who do not receive help in taking their medication have a risk of 2.23 of not adhering to treatment compared with patients who do receive help in taking their medication. Drug use and compliance with anti-COVID-19 barrier measures did not significantly affect treatment adherence. However, experiencing a discriminatory attitude from family and friends and not receiving assistance in medication were identified as significant risk factors for non-adherence. These findings emphasize the crucial role of social dynamics, support networks, and the patient's immediate environment in influencing adherence to complex treatment regimens, especially in the context of co-infection with TB and HIV. Addressing these social determinants can be vital in enhancing overall treatment adherence.

Table 5. Clinical characteristics (Bivariate).

Characteristics	Adherence (%)	OR	CI at 95%	p-value
Type of cohort				0.029
• During COVID-19	75 (72.8)	1	-	
• Before COVID-19	65 (58.6)	1.90	1.10 - 3.37	
Type of tuberculosis				0.317
• Extra-pulmonary	23 (74.2)	1	-	
• Pulmonary	111 (64.9)	1.55	0.65 - 3.69	
Knowledge of treatment duration				0.509
• Yes	125 (64.4)	1	-	
• No	6 (54.5)	1.51	0.44 - 5.13	
Presence of undesirable effects				<0.001
• Yes	67 (50.0)	9.14	3.91 - 21.40	
• No	64 (90.1)	1	-	

Table 6. Family characteristics and habitat (Bivariate).

Characteristics	Adherence (%)	OR	CI at 95%	p-value
Attitude of family/relatives				0.008
• Discriminatory	17 (44.7)	2.66	1.30 - 5.45	
• Not discriminatory	114 (68.3)	1	-	
Help with taking medication				0.010
• Yes	99 (69.7)	1	-	
• No	32 (50.8)	2.23	1.21 - 4.10	
Drug use				0.442
• Yes	10 (55.5)	1	-	
• No	121 (64.7)	0.68	0.26 - 1.81	
Compliance with anti-COVID-19 barrier measures				0.114
• Yes	105 (66.5)	1	-	
• No	20 (52.6)	1.78	0.87 - 3.65	

4. Discussion

The survey conducted in health facilities in the East region of Cameroon reveals that female participants outnumbered male participants prior to COVID-19. This result is contrary to the one presented by Kettani *et al.* (2018) [6], where male individuals (30 participants) were more numerous than female individuals (16 participants). This difference could be explained by the fact that the studies by the former authors were limited to one hospital, whereas this current study was carried out in several health facilities in the East region of Cameroon.

The female predominance observed in this study does not corroborate with the study by Noubom *et al.* (2013) [7] where the female population represented 35.2% of the total population, whereas the male population was much higher with a percentage of 64.8%. This difference can be explained by the fact that the population (2556 participants) in that study is much larger than this one, and also by the fact that the data were collected over a longer period, i.e. 10 years. This female predominance runs counter to the results obtained by Pefura Yone *et al.* (2012) [8] at the Jamot Hospital in Yaoundé. In their study, 57% of participants were men. In this case, the male predominance can be explained by socio-cultural factors such as polygamy [9].

However, this predominance of women is in line with the study by Tékpa *et al.* (2019) [10], who showed that tuberculosis affects women earlier than men, stating that the age group most affected among women was 25 to 34 years (46.09%), while 36.96% of men were aged 35 to 44 years. Furthermore, the high proportion of women observed in this study could be due to the population of hospitalised patients, which is characterised by a predominance of HIV-infected women [10]. The predominance of females observed in this study was much more noticeable in health facilities prior to COVID, whereas during COVID there was a predominance of males.

The predominance of the male population observed during COVID-19 corroborates with Kettani *et al.* (2018) [6], who described a predominance of males during their study. This predominance of co-infected male patients was 63%, with a dominant age range between 30 and 39 years. This result could be different from that of the study conducted in eastern Cameroon, as the population was smaller (117 people), and the study by Kettani *et al.* (2018) [6] was not carried out on the basis of a cohort, but rather was a retrospective cross-sectional descriptive study. The male predominance during COVID-19 also corroborates with the study by Dabo *et al.* (2022) [11]. They obtained a sex ratio of 1.6 in favour of males. However, this study is also a descriptive study like that of Kettani *et al.* (2018) [6]. This result is contrary to that of Traoré (2020) [12], who had a female population of 71.3%, with a sex ratio of 2.5 in favour of the female population. According to this author, this result can be explained by the fact that: anatomically, the contact surface for women is larger than for men (which makes them more vulnerable to HIV), socially by the fact that the study was conducted in a predominantly polygamous society in which men tend to go to fewer health facilities.

The mean age was 39.3 ± 11.4 years with a sex ratio of 1.33 in the cohort during COVID-19. Several authors have reached the same conclusions regarding male predominance [13] [14] [15] [16]. In this case, young men are the most affected by the double burden of HIV and TB. They represent the most sexually active and productive segment of the population. The fact that there are more co-infected men than women could be explained by the fact that women in this part of the country are tested for HIV earlier than men, because they have to give birth at a relatively young age, and so benefit from being tested for TB in cases of seropositivity.

In our study, we found that the marital status of married patients was significantly associated with TB followed by single patients. Divorced or widowed patients were less likely to develop TB than married and single patients, which are consistent with Mitku *et al.*'s study in Ethiopia in 2016 [17]. The explanation we can give for this is that single patients are much younger and have a different lifestyle to the other groups.

This study showed that around 93% of patients had at least primary school education. We found that there was no statistically significant association at the 5% significance level between educational level and adherence to treatment (p-value = 0.121). This result is contrary to the findings of Issoufi in 2008 [18]. He observed that patients with a high level of education are associated with good adherence to programmes to combat these diseases. Their various studies confirm this hypothesis. 46.2% of patients have an income of less than 50,000 francs. Free treatment is fundamental to adherence, given the vulnerabilities associated with the social integration of people affected by the disease. Health services therefore need to pay particular attention to understanding patients' needs [5].

Clinical characteristics (before and during COVID-19)

The table showing the clinical characteristics before and during COVID-19 shows that only patient status (p = 0.033) is not identically distributed, whereas the other variables are identically distributed. These are: patient outcome (p = 0.171), type of tuberculosis (p = 0.539), treatment protocol (p = 1.0), knowledge of duration of treatment (p = 0.769), knowledge of adverse effect (p = 0.924).

Patient status shows that there were 108 new patients before COVID-19, and 98 after it. As for relapses, there was one patient before COVID-19 and seven patients after it. This situation could be explained by the theories of reasoned action and the Health Belief Model. The patients who joined the cohort would have done so because they thought it would enable them to achieve the goal they were seeking, i.e. a better state of health, a better understanding of their illnesses, or better control over the risk factors that could aggravate their state of health. Patients who relapsed could have done so because they did not believe in the treatment's ability to provide a solution to their ailments, or because they did not feel able to exercise control over their illnesses, being influenced by the opinions of their environment.

In this study, the pulmonary location of tuberculosis was 84.9%, which is far from the result (56.5%) obtained by Soumaré *et al.* in Bamako (2012) [15]. This difference could be explained by the difficulty of diagnosing extra-pulmonary tuberculosis, as the technical facilities are limited to microscopy, which makes it difficult to diagnose extra-pulmonary forms. 65.4% of patients surveyed stated that they had experienced adverse effects related to their treatment. This result is slightly different from the 42% obtained by Berkchi *et al.* (2020) [19]. These adverse effects could be explained by the possible interaction between antiretroviral and anti-tuberculosis treatments.

Family characteristics and habitat (before and during COVID-19)

From the table showing family characteristics before and after COVID-19 we observe that only compliance with barrier measures against COVID-19 (p = 0.006) did not change identically, while all the other variables changed identically, namely: family attitude (p = 0.744), help with taking medication (p = 0.916) and drug use (p = 0.983).

The table showing family characteristics shows that compliance with barrier measures slackened after COVID-19. It can be seen that before the pandemic, 27.4% of participants complied with the barrier measures, but after the pandemic, only 11.9% of participants complied with these measures. This relaxation in compliance with barrier measures may be explained by the fact that participants may have believed that the consequences of the disease were no longer serious, or that the pandemic had completely disappeared, an argument derived from the Health Belief Model that may explain this situation. They could also have been slack in applying the barrier measures, because they might have felt discouraged from applying the measures, as they would not have been able to cure their co-infection; this argument is in line with social cognitive theory.

Level of therapeutic adherence in co-infected patients

The graph describing the distribution between patient adherence and cohort type shows that the distribution is not identical (p = 0.007). Patients could have considered that hospitals during the COVID-19 period were inappropriate for providing solutions to their health problems, because they would have been subject to a heavy workload generated by the arrival of people infected by COVID-19. What about fear of contracting COVID-19 at hospital or obligatory testing foe COVID at Hospital? This situation is alarming because tuberculosis and HIV are major causes of mortality and morbidity worldwide. Indeed, tuberculosis remains a major public health problem worldwide, and in 2020 was the second leading cause of death due to a single infectious agent, after COVID-19. The World Health Organisation's "Stop TB" strategy aims to achieve, by 2035, a 95% reduction in mortality and a 90% reduction in the incidence of tuberculosis compared with 2015 [20]. Tuberculosis has also joined the effects of the COVID-19 pandemic, so that for the first time in more than a decade, a net increase in deaths and an increase in the number of new cases have been observed [20]. It is therefore important to make every effort to combat HIV and tuberculosis. Worldwide, HIV-tuberculosis co-infection is a major public health problem, and the real problems it poses are diagnostic and therapeutic, with the difficulty of confirming tuberculosis microbiologically [11].

The graph describing patient adherence to treatment according to division shows that there is no identical distribution between the variables (p < 0.001). The divisions where patients adhered more to treatment were the following: Kadey (100%), Lom et Djérem (76.8%), Boumba et Ngoko (75%), and Haut Nyong (29.8%). This adherence by patients in the divisions may be due to the fact that health workers have done enough to raise awareness of HIV-TB co-infection, which could have motivated patients to take action by coming to the health facilities in order to follow up their treatment. This situation could also be explained by the fact that people who adhere more in these divisions are in families where they are supported by their relatives during their treatment. As tuberculosis is a stigmatized disease in society [21], co-infected people need the support of their families [22].

Factors responsible for treatment adherence

Bivariate analysis of socio-demographic factors with adherence shows that only the following variables: religion (p < 0.001), residence (p = 0.008), type of health facility (p < 0.001), distance from residence/FOSA (p = 0.012) are not identically distributed.

Lay people were six times more likely to adhere to treatment than Christians and Muslims. The situation of lay people can be explained by the theory of reasoned action: they may believe in the action of the health services, and therefore feel safe taking the treatment, whereas Christians and Muslims may be influenced by other therapeutic routes such as mosques and churches, and these different routes may therefore prevent them from adhering to the treatment.

The predominance of participants in this study in urban areas is in agreement with that of Yehia *et al.*'s study (2015) [23], the latter obtained a strong domination of populations living in urban areas. However, this result can be explained by the fact that this research was carried out in an urban area in a University Hospital Centre (CHU). With regard to income, patients with an income of less than 50,000 CFA francs were one time more likely to adhere to the treatment than others with higher incomes, a result that can be explained by the theory of reasoned action. People with an income of less than 50,000 CFA francs would choose to put their health first, rather than their comfort. In the same way, people living in rural areas are twice as likely to adhere to treatment as people living in urban areas, as they would consider it a privilege to be in possession of care or treatment that they do not always have the opportunity to have.

Patients attending public hospitals were nineteen times more likely to adhere to treatment than those attending private facilities. This may be because these patients may be better treated in these facilities than in private ones. Similarly, patients living more than 10 km from health facilities were twice as likely to adhere to treatment, possibly because they were more motivated to receive treatment than those living closer to health facilities.

Clinical characteristics (Bivariate)

Analysis of clinical characteristics with adherence showed that for all variables the only variables that were not identically distributed were: follow-up cohort ($p = 0.029$), adverse event ($p < 0.001$). People who had joined the cohort before COVID-19 were 1.9 times more likely to adhere to treatment. Individuals who had experienced adverse events and who knew about them were 9.1 times more likely to adhere to treatment, a result in line with the theory of reasoned action. Individuals' actions are guided by knowledge that enables them to act favorably or unfavorably, depending on the goal they wish to achieve.

Family characteristics and habitat (Bivariate)

Analysis of family characteristics and adherence showed that two variables were not distributed identically: the attitude of family carers ($p = 0.008$) and help with taking medication ($p = 0.010$).

People who experience discriminatory attitudes on the part of their family or friends are 2.6 times more likely to adhere to treatment than those who do not, and not receiving help with taking medication is associated 2.2 times more with adherence to treatment. This suggests that people who do not receive help from their family or friends, or who experience discriminatory attitudes, may rely on their knowledge of the disease to motivate them to take the treatment.

5. Conclusion

This study highlights the factors of therapeutic adherence in the COVID-19 context among HIV-TB co-infected patients. By comparing the pre-COVID cohort with the post-COVID cohort, this study reveals that, among factors linked to patient, treatment and the environment, religion, the type of health facility attended by the patient, the distance of residence from the health facility, the presence of side effects, COVID-19, the attitude of the family or close friends and assistance in taking medication are risk factors influencing adherence to treatment among HIV-TB co-infected patients.

Compliance with Ethical Standards

We obtained authorization to collect data from the regional public health delegation of the East.

Authors' Contributions

François Anicet ONANA AKOA, Ulrich DAMA, Jean NDIBI ABANDA, Alphonse TEDONGE ASOBOCHIA, Melkior FOBASSO DZEUTA, Pearl NSOM MBU, Yokyu Zachary PANGWOH, and Pierre YASSA YONIENE designed the study, François Anicet ONANA AKOA and Pierre YASSA YONIENE analyzed the data and produced the first draft of the study. All authors extracted the manuscript and approved the final draft.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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