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Biological Monitoring of Patients under First-Line Antituberculous Treatment in Chad from 2021 to 2022

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Abstract

Tuberculosis (TB) remains a major public health challenge in Africa, particularly in Chad. The success of first-line antituberculous treatment relies on rigorous clinical follow-up and regular laboratory monitoring. This study aims to assess the biological follow-up of patients undergoing first-line antituberculous treatment in Chad, using a large provincial cohort and a prospective hospital cohort at the CHU-RN, to inform strategies for improving TB management in Chad. A mixed cross-sectional retrospective and prospective study was conducted using data from TB treatment centers across ten Chadian provinces from January 2021 to June 2022, along with samples collected at CHU-RN in N'Djamena from March to September 2021. Data included demographic, clinical, and biological information from patients under first-line antituberculous treatment. Biological monitoring was assessed according to the recommendations of the National Tuberculosis Control Program (PNT) of Chad and the WHO. Among 5,811 provincial patients, the overall performance rate

of recommended biological tests (AFB smear and GeneXpert) was 52.8%, with GeneXpert performed in only 5.1% of cases and rifampicin resistance detected in 3.36% of those tested. At CHU-RN, 111 patients were enrolled, and 95.5% received biological monitoring consistent with guidelines, although follow-up markedly declined after the second month. Follow-up was particularly inadequate among men, patients with low levels of education, or those without health insurance, but these associations were not tested using multivariate analysis. Biological follow-up of patients on antituberculous therapy in Chad remains insufficient, potentially compromising treatment efficacy and promoting resistance emergence. Strengthened strategies targeting vulnerable populations and improved access to care are essential to enhance biological monitoring and TB treatment outcomes in Chad.

Keywords

Tuberculosis, Diagnosis, *Mycobacterium tuberculosis*, Epidemiology

1. Introduction

Tuberculosis (TB) continues to be a critical public health issue, especially in resource-limited countries of sub-Saharan Africa, where incidence and mortality rates remain high. According to the World Health Organization (WHO), TB is a priority in Chad, with an estimated incidence rate of 139 cases per 100,000 population in 2023 [1]. The standard treatment protocol, combining a four-drug antituberculosis regimen over six months, demands close clinical and biological supervision to evaluate treatment efficacy, promptly identify drug resistance, and monitor adverse reactions [1]. Biological monitoring principally involves detection of Acid-Fast Bacilli (AFB) in sputum, molecular resistance testing, and cultures, which are crucial to ensuring effective care and preventing the emergence of resistant strains. Despite clear national guidelines, biological follow-up in Chad is hindered primarily by human, material, and financial resource limitations. This study aims to evaluate the compliance of biological monitoring among patients undergoing first-line TB treatment in Chad from 2021 to 2022, focusing particularly on patients at the Centre Hospitalier Universitaire de Référence Nationale (CHU-RN) of N'Djamena. Findings from this investigation may inform improvements in biological monitoring strategies and strengthen TB control efforts in Chad.

2. Materials and Methods

2.1. Study Design

This mixed descriptive study combined retrospective data analysis from TB treatment centers in Chad (N'Djamena and other regions) between 2021 and 2022 with a prospective component conducted at CHU-RN from March to September 2021. The cities concerned were Abéché, Am-timan, Bol, Fada, Koumra, Laï, Massenya,

Moussoro, N'Djamena and Sarh. CHU-RN represents the largest TB treatment center in Chad. The provincial data constituted a large retrospective cohort, whereas patients enrolled at CHU-RN formed a smaller prospective hospital cohort.

2.2. Study Population

The study population included all adult patients (aged 15 years and above) treated with first-line antituberculous drugs and managed for pulmonary tuberculosis at the study sites during the study period.

2.3. Data Collection

The data were collected using a standardized questionnaire. Sputum samples were collected from patients followed at CHU-RN and analyzed at the Mycobacteriology Laboratory of CHU-RN and the Bacteriology Laboratory of CHU Arnaud de Villeneuve in Montpellier, France.

The data collected include demographic data (age, sex and place of residence), clinical data (TB type, history, HIV status), biological data (BAAR, GeneXpert, culture, antibiogram), therapeutic data (treatment regimen, duration of treatment and compliance) and evolutionary data from treatment (relapse and failure).

2.4. Biological Monitoring

Biological monitoring was assessed based on the examinations recommended in the national TB control guidelines of Chad. These include sputum AFB smear microscopy and molecular resistance testing for antituberculous drugs. For new smear-positive pulmonary TB cases, sputum smears are recommended at month 2, month 5 and month 6 (end of treatment) [2]. If the patient cannot produce sputum at the end of treatment, a final smear should nevertheless be performed on saliva. Patients who remain smear-positive at month 2 continue to the continuation phase with an additional control at month 3, without prolongation of the intensive phase. Biological monitoring was considered adequate when patients completed at least 80% of the expected smears according to this schedule (at months 2, 5 and 6, and at month 3 when indicated).

2.5. Laboratory Analyses

Laboratory evaluation was performed exclusively on samples collected at CHU-RN. Sputum samples from each enrolled patient were decontaminated with the Mycoprep® kit and cultured on solid (Lowenstein-Jensen) and liquid (MGIT) media. Direct examination was conducted pre- and post-decontamination. GeneXpert MTB/RIF Ultra molecular testing identified *Mycobacterium tuberculosis* complex (MTBC).

2.6. Statistical Analysis

Data entry was performed using Microsoft Excel, and statistical analyses were executed with SPSS v2.0. Categorical variables were described by frequencies and

percentages, and continuous variables by mean and standard deviation.

3. Results

3.1. Results from Patients Treated in Chadian Provinces

The study included 5811 patients treated for pulmonary tuberculosis, including 118 children under 15 years, from several provinces during 2021-2022 (Table 1). The median age was 33 ± 13 years, with a male predominance (70.8% men vs. 29.2% women).

Table 1. Age distribution.

Age	n	%
[0 - 4]	19	0.37
[5 - 14]	99	1.93
[15 - 24]	1100	21.46
[25 - 34]	1459	28.46
[35 - 44]	1095	21.36
[45 - 54]	688	13.42
[55 - 64]	347	6.77
≥65	319	6.22
Total	5126	

3.1.1. Biological Characteristics

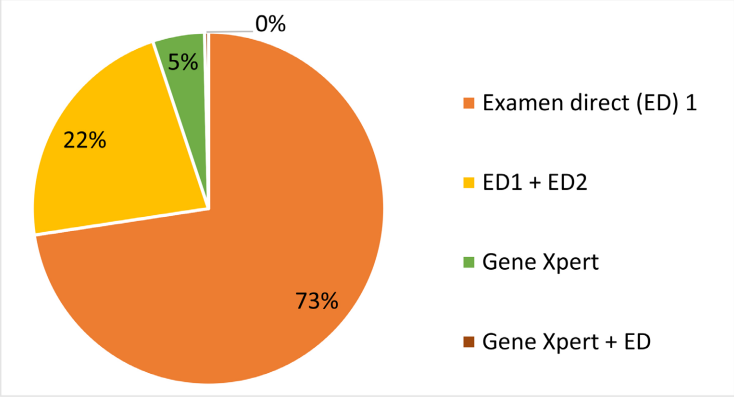

Figure 1. Completion rate of the various biological tests.

The overall performance rate of recommended biological tests (AFB smear, GeneXpert) was approximately 52.8%. Figure 1 highlights test distribution, showing that most follow-ups involved a single microscopy examination (73%). Among 5513 microscopy tests conducted, 15.71% (866 patients) were positive. GeneXpert testing was performed on 298 patients (5.13%), identifying 243 MTB-positive cases: 78.19% rifampicin-sensitive, and 3.36% rifampicin-resistant. Multidrug-Resistant (MDR) cases were distributed across 5 of the 10 studied provinces (Figure 1). Figure 2 shows the distribution of MDR cases by city.

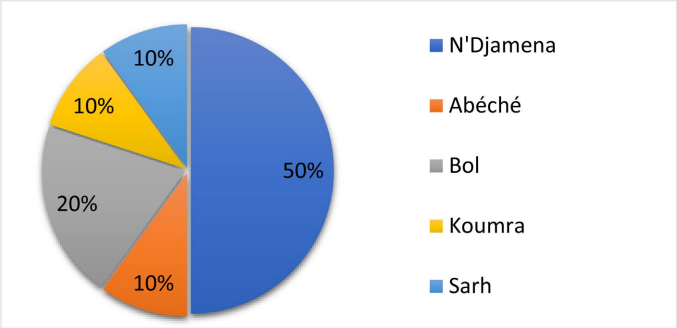

Figure 2. Distribution of MDR cases by city.

3.1.2. Clinical and Therapeutic Characteristics

Most patients (94.9%) had smear-positive pulmonary tuberculosis. A minority (5.1%) reported TB history or comorbidities like diabetes and hypertension. HIV status was available for only 15 patients; one (6.67%) was co-infected. Two HIV-negative patients experienced treatment failure (both from Abéché); they had positive smear microscopy but negative Xpert MTB/RIF Ultra results, findings consistent with Non-Tuberculous Mycobacteria (NTM). Biological monitoring was predominantly concentrated in the first two months (40.62% of controls), declining in later phases (data for 578 patients). Treatment failure rate was 5.36%, relapse rate 0.69% (Table 2). Among failures, two cases involved nontuberculous mycobacteria diagnosed by microscopy but not GeneXpert.

Table 2. Distribution of biological results by follow-up period.

Monitoring period*	Negative		Positive		Total	
	n	%	n	%	n	%
C1	0	0	2	0.03	2	0.03
C2	215	3.7	17	0.29	232	3.99
C3	14	0.2	0	0	14	0.24
C4	1	0.02	0	0	1	0.02
C5	150	2.6	11	0.19	161	2.77
C6	155	2.7	7	0.12	162	2.79
C7	1	0.02	0	0	1	0.02
C8	2	0.03	1	0.02	3	0.05
Monitoring and follow-up	4159	71.6	1041	17.91	5200	89.49
Failure	7	0.1	24	0.41	31	0.53
Relapse	0	0	4	0.07	4	0.07
Total	4704	80.9	1107	19.1	5811	100

*C1: Control at month 1 after treatment, C2: Control at month 2...C8: at month 8.

Concerning the cities of Chad, after N'Djamena, the cities of Bol, Koumra and Abéché, respectively, evaluate follow-up biological controls on their patients (Ta-

ble 3). The CHU-RN alone followed 88.2% of the patients in the study. Overall, the number of biological controls carried out on the patients by month is presented in Figure 3.

Table 3. Biological results by city.

City	Negative		Positive		Total	
	n	%	n	%	n	%
Abéché	137	2.4	30	0.5	167	2.9
Am-Timan	37	0.6	2	0.03	39	0.7
Bol	231	4.0	12	0.2	243	4.2
Fada	5	0.1	3	0.1	8	0.1
Koumra	177	3.0	15	0.3	192	3.3
Laï	9	0.2	4	0.1	13	0.2
Massenya	10	0.2	6	0.1	16	0.3
Moussoro	0	0	1	0.02	1	0.0
N'Djamena	4094	70.5	1030	17.7	5124	88.2
Sarh	2	0	6	0.1	8	0.1
Total	4702	80.9	1109	19.1	5811	100

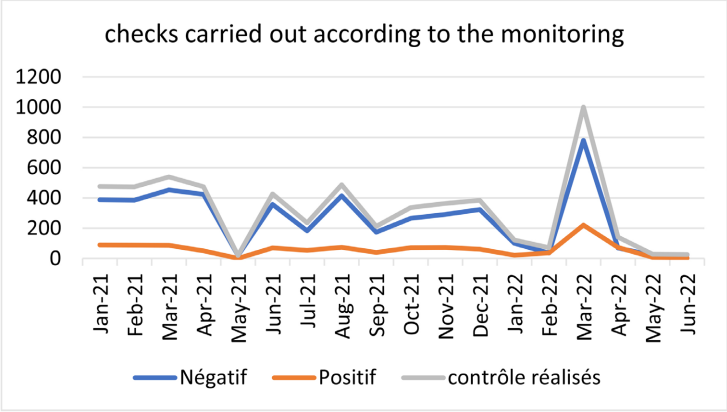

Figure 3. Number of checks carried out by month.

3.2. Results among Patients Followed at CHU-RN

One hundred eleven patients were enrolled; mean age was 35 years (±13), range 16 - 85; median 33 years; 70.3% male. Most resided in central N'Djamena (79.2%), followed by peripheral neighborhoods and 4.2% from villages.

3.2.1. Biological Follow-Up

Among these, 61.2% underwent follow-up at months 5 and 6, while 34.2% attended the 2-month check-up. The CHU-RN displayed markedly higher adherence (95.5%). Table 4 depicts patient distribution by month of biological monitoring post-treatment initiation.

Table 4. Follow-up months distribution.

Number of months of follow-up	n	%
2-month follow-up	38	34.2
3-month follow-up	3	2.7
4-month follow-up	2	1.8
5-month follow-up	40	36.0
6-month follow-up	28	25.2
Total	111	100

Mycobacterial test results revealed positive AFB sputum smear tests in 3.6% of cases, positive AFB pellet smear tests in 5.4% of cases, and rifampicin resistance detected in 6.52% of cases (Table 5). A discrepancy between pre- and post-decontamination microscopy was noted in 7.2%, with 92.8% concordance.

Table 5. Results of the mycobacteria detection test.

Mycobacteria detection	n	%
ED-Auramine Sputum	111	
Positive	4	3.6
Negative	107	96.4
ED-Auramine Culot	111	
Positive	6	5.4
Negative	105	94.6
Xpert MTB Ultra	111	
MTB Not Detected	65	58.6
MTB Detected	43	41.4
Detected High	7	6.31
Detected Medium	8	7.21
Low Detected	20	18.02
Very Low Detected	3	2.70
Trace Detected	8	7.21
Rifampicin resistance	46	
Detected	3	6.52
Not Detected	37	80.43
Undetermined	6	13.04

3.2.2. Culture and Drug Susceptibility

Of 111 cultures, 18.9% were positive, 75.7% negative, and 5.4% contaminated. Antibiograms were valid for 18 of 21 performed (86%). Among positive cultures, 33.33% showed resistance to first-line antituberculous drugs (Table 6).

Table 6. Results of susceptibility tests to first-line antituberculous drugs.

Drug Resistance	n	%
Sensitive SIRE-PZA	12	66.67
RIF mono resistance	1	5.56
Single resistance to INH	1	5.56
RIF-INH-STR-EMB resistances	1	5.56
INH-PZA resistances	2	11.11
RIF-INH resistances	1	5.56

4. Discussion

This study revealed that only 52.8% of patients across ten provinces had adequate biological monitoring, corroborating findings from other sub-Saharan African settings where adherence frequently remains insufficient [3]. Ngahane *et al.* [4] in Cameroon reported a similar 54% adherence, while Abay *et al.* [5] in Ethiopia found 67%. Socioeconomic and geographic determinants such as low social coverage, remoteness from diagnostic and treatment centers, and low education hinder access and compliance, as also reported elsewhere [3] [6].

The CHU-RN displayed markedly higher adherence (95.5%), undoubtedly reflecting centralized quality care, access to adequate equipment and appropriately trained staff. Our study showed that the CHU-RN is the largest center in the country for TB care. In our study, overall patient follow-up at CHU-RN represented 88.2% of cases. However, the situation remains mixed in the periphery where monitoring remains partially deficient due to a lack of equipped laboratories, a shortage of qualified personnel, limited access to molecular tests and variability in compliance with control schedules. Furthermore, the significant drop in biological monitoring after the first two months, observed in our study group, likely explains the decrease in follow-up visits observed in our cohort, which corroborates the study by Mukadi *et al.* [7] (2023) in Uganda. This situation highlights the critical importance of adherence to follow-up during the prolonged course of treatment. This lack of follow-up contributes to bacterial persistence and the development of resistance, as evidenced by the discovery of rifampicin resistance in patients, even at the beginning of treatment (3.36% resistance identified by GeneXpert). Cases of Nontuberculous Mycobacteria (NTM) undetected by GeneXpert but positive on microscopy stress the need for complementary diagnostics per recent WHO recommendations [8]. TB/HIV co-infection is a major problem, and international guidelines recommend systematic HIV testing for all TB patients. HIV status was documented for only 15/5811 patients in the provincial cohort (0.26 %), with one HIV/TB co-infected case (6,67%). Togde *et al.* [9] reported a 7.4% TB/HIV co-infection rate at CHU-RN, highlighting that the extremely low proportion observed in our study mainly reflects missing HIV data rather than a truly low burden. HIV coinfection, although infrequently documented here, has been associated with poorer monitoring and outcomes in comparable settings [10] [11]. Follow-up was particularly inadequate among men, patients with low levels of edu-

cation, or those without health insurance, but these associations were not tested using multivariate analysis. GeneXpert only detects the *Mycobacterium tuberculosis* complex and can therefore be negative in cases of NTM, while microscopy remains positive, underscoring the need for culture and species identification when treatment failure is suspected. Without these tools, patients may remain on inappropriate TB regimens, with unnecessary toxicity and delayed NTM-specific management. Material limitations like uneven distribution of equipped labs call for enhanced decentralized capacities to minimize loss to follow-up. Alarmingly, one-third of positive cultures exhibited resistance to first-line drugs, signaling an urgent need for strengthened surveillance and MDR-TB management in Chad, consonant with WHO 2024 guidelines [8]. Microscopy discordance between pre- and post-decontamination in 7.2% of cases highlights the need for training and improved laboratory protocols. Decentralizing GeneXpert to district hospitals at the primary level of the Chadian health system is essential to extend biological monitoring beyond provincial capitals [12] and avoid penalizing patients who cannot afford referral-level travel.

5. Conclusion

Biological monitoring is better at CHU-RN than in provincial settings but remains insufficient over time, with a sharp drop in follow-up after the second month. Provincial and rural areas face particularly marked deficits, which impede treatment success, promote resistant TB forms and pose critical public health threats. Decentralizing GeneXpert to district hospitals, combined with continuous healthcare worker training and innovative patient-engagement strategies, is essential to ensure equitable biological monitoring and effective TB control across Chad.

Ethical Considerations

This study received approval from the Ministry of Public Health and Prevention of Chad (number 4238/MSPSN/SE/DG/DGTPRC/DPERO/SRO/2020) and from the Ministry of Scientific Research. Patient informed consent was waived given the anonymized data collected during routine care.

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Conflicts of Interest

The authors declare no conflict of interest. The study was funded by the French

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