

Therapeutic Compliance in Patients Followed for Lupus and Rheumatoid Arthritis in Niamey (Niger): Multicenter Study

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Abstract

Introduction: Like all chronic diseases, Autoimmune diseases (AID) require long-term, even lifelong, medication. Their progression and prognosis depend on adherence to these therapies, which are often fraught with side effects. We conducted a study on the adherence of patients being treated for systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). **Method:** Our study was prospective, descriptive and analytical, lasting 3 months from May 20, 2024, to August 20, 2024, in the 3 reference hospitals of Niamey. **Results:** A total of 27 patients were included, representing 30% of the patients with lupus and/or rheumatoid arthritis collected. The age group over 35 years was the most represented, with a frequency of 74.1% (n = 20) and a female predominance of 92.60% (n = 25). Prednisone and hydroxychloroquine were the most used molecules, 70.4% each, followed by methotrexate at 22.2%. Low adherence predominated, followed by medium adherence and high adherence in 67% (n = 18), 26% (n = 7) and 7% (n = 2) respectively. Adherence to antimalarials was the lowest, followed by glucocorticoids and immunosuppressants in 51.9% (n = 14), 48.1% (n = 13) and 25.9% (n = 7). Patients with SLE had lower adherence at 44.4% (n = 12). The major barriers to treatment adherence reported by our patients were weariness, forgetfulness, fear of side effects and low socioeconomic level in 51.9% (n = 14), 48.1% (n = 13), 40.7% (n = 11) and 29.6% (n = 8), respectively. **Conclusion:** It is important that physicians adopt a prescribing strategy that focuses on limiting themselves to the essentials, prioritizing single-dose molecules and fixed combinations if necessary.

Keywords

Therapeutic Compliance, Lupus, Polyarthritis, Niger

1. Introduction

Autoimmune diseases (AID) constitute a heterogeneous group of more than 100 diseases, affecting 5% to 8% of the world's population and constituting the 3rd cause of morbidity in developed countries [1]. In Africa, they have long been considered rare, even non-existent, because they are unknown and under-diagnosed due to the great variability of their mode of revelation, the often-misleading nature of their inaugural presentations and the inadequacy of the technical platform. This explains the scarcity of the bibliography on these diseases south of the Sahara [2].

In Senegal, Diallo S *et al.* reported 3602 observations of systemic diseases, representing a hospital prevalence of 2.6% from 2010 to 2022 [3]. African League Against Rheumatism in 2013 revealed that 20% of these clinicians (spanning rheumatology, general practice, nephrology and dermatology) had seen more than 50 new patients with SLE in the previous 12 months, indicating that the incidence of this condition is not negligible [4]. In Niger, the first cases of RA and SLE were published in hospitals in 2009 and 2015. Since these preliminary studies, several others have been published, attesting to the increasing incidence of these pathologies with the improvement of diagnostic conditions (specialists, equipment) [5]-[7].

Treatment is based on corticosteroids during relapses and immunosuppressants or immunomodulators for background therapy. This background treatment is usually prescribed for life. Their progression and prognosis depend on adherence to prescribed treatment regimens, which are often marred by side effects, in addition to the constraints of their daily use and the cost in our countries.

A study on overall adherence of patients with chronic illness in the Democratic Republic of Congo shows poor adherence (10%). Factors associated with nonobservance of treatment among the respondents were the low level of financial income, the lack of control over the timetable set for treatment, the difficulties of accessibility to drugs, and the long duration of treatment and negligence of the sick treatment [8].

To our knowledge, few studies have been conducted on adherence in autoimmune diseases.

In this context, we propose to study the compliance of patients followed for lupus and rheumatoid arthritis in Niamey hospitals.

2. Patients and Methods

Our study was conducted in internal medicine consultations in the 3 reference hospitals of Niamey: Amirou Boubacar Diallo National Hospital, Niamey National Hospital, General Reference Hospital. We also conducted home and tele-

phone interviews according to the availability of patients. This was a prospective descriptive and analytical study lasting 3 months, from May 20, 2024 to August 20, 2024.

The study population was represented by all patients followed for systemic lupus erythematosus (SLE) and/or rheumatoid arthritis (RA) during the study period.

To be included in the study, patients should meet the following criteria: Give verbal consent, be in remission; be followed as an outpatient; be under treatment for at least 6 months. They did not include patients who did not give their consent, patients in flare-ups, patients aged under 18 years and pregnant women.

We interviewed patients face-to-face at the hospital and at home to fill in the forms. For patients we were unable to see face-to-face, we conducted the interview over the telephone if they gave their consent.

We assessed socio-economic status on the basis of patients' monthly income and whether or not they had health insurance [9].

- **Assessment of knowledge and compliance**

- **On knowledge of the treatment:** To assess knowledge of the treatment, in the absence of a “Gold Standard”, we used the 3 criteria most often used in the literature:

- Know how to cite the name or International Common Name (INN) of the medicine;
- Know the indication: its Marketing Authorization (MA) or its mechanism of action or the target organ;
- Know the administration instructions: number of tablets to take and the time of day. The correct answer was the time of day without specifying the schedule or recommendations (fasting, during meals, etc.).

Each drug line was rated out of 3 points (1 point per item known). Analysis of the responses made it possible to distinguish 3 levels of knowledge:

- Perfect knowledge of the treatment if the patient obtained a score of 3/3;
- Good knowledge of the treatment for a score between 1.5 to 3;
- Poor knowledge of the treatment for a score less than or equal to 1.5/3.

- **On treatment adherence:** we used the Morisky-Green score [Morisky Medication Adherence Scale-8 (MMAS-8)] (**Table 1**).

The MMAS-8 is a self-report questionnaire consisting of 8 questions (items). The questions have been formulated to avoid a “yes” bias, *i.e.*, the wording of item 5 is reversed to avoid the tendency to respond specifically to a series of questions regardless of their content. The response options are yes or no for items 1 to 7 and a 5-point Likert response scale for the last item. Each “no” response is scored “1” and each “yes” is scored “0” except for item 5, in which each “yes” response is scored “1” and each “no” is scored “0”. For item 8, if a patient chooses the response “0”, the score is “1” and if he chooses the response “4”, the score is “0”. Responses “1, 2, 3” are respectively scored “0.25; 0.50; 0.75” [3].

The total MMAS-8 score can range from 0 to 8, with scores < 6; 6 to 7 and 8 reflecting low, medium and high adherence, respectively.

Table 1. Morisky Medication Adherence Scale with 8 items (MMAS-8) [10].

1. Do you sometimes forget to take your medication?	Yes No
2. People sometimes forget to take their medication for reasons other than forgetting. Thinking back over the past two weeks, were there any days when you didn't take your medication?	Yes No
3. Have you ever reduced or stopped taking your medication without talking to your doctor because you felt worse when you took it?	Yes No
4. When you travel or leave home, do you sometimes forget to bring your treatment with you?	Yes No
5. Did you take your medicine yesterday?	Yes No
6. When you feel your illness is under control, do you sometimes stop taking your medication?	Yes No
7. Taking medication on a daily basis can be a real hassle for some people. Have you ever felt uncomfortable sticking to your treatment plan?	Yes No
8. How often do you have trouble remembering to take all your medications?	0. Never/Rarely 1. Regularly 2. Sometimes 3. From time to time 4. All the time

Data from each patient were collected using a pre-established questionnaire. Data analysis was performed using Sphinx software version 5.1.0.4. We used the *Chi-Square* (X^2) test to compare variables, with a significance level of $p < 0.05$.

3. Results

A total of 90 patients were identified in the 3 hospitals. At the end of the selection, 27 patients met the inclusion criteria, representing 30% of patients with Systemic Lupus Erythematosus (SLE) and/or rheumatoid arthritis (RA). A total of 16 patients had SLE, 10 had RA, and 1 patient had Rhupus (SLE + RA combination).

The majority of participants were women, 92.6% ($n = 25$) with a sex ratio M/F of 0.08. The mean age of patients was 45.33 ± 13.55 years [range (25 - 75)]. The age group over 36 years was the most represented with a frequency of 74.1%. High blood pressure was the most represented comorbidity in 44.40% ($n = 12$).

Corticosteroids were used in 81.5% ($n = 22$) compared to other therapeutic classes. Hydroxychloroquine and prednisone were the most used molecules in 70.4% ($n = 19$) each.

The mean duration of treatment was 8.33 ± 5.08 years [range (7 - 24 months)]. The durations between 6-10 years were the most common with a frequency of 25.9% each.

Some patients could take more than 8 tablets per day and all (100%) took their treatment orally and the majority, 70.40% (n = 19) had a twice-daily administration frequency and (2) patients took more than 8 tablets per day (see **Table 2** & **Table 3**).

Table 2. Distribution of patients according to the number of medications.

Number of medications	Effective	Percentage (%)
1 - 2	4	14.8
3 - 5	16	59.3
6 - 8	7	25.9
TOTAL	27	100

Table 3. Distribution of patients according to the number of daily tablets.

Number of daily tablets	Effective	Percentage (%)
1 - 2	2	7.4
3 - 5	16	59.3
6 - 8	7	25.9
Greater than 8	2	7.4
TOTAL	27	100

Treatment awareness and compliance. Eighteen patients were able to provide the names of their medications, or 67%, but only 22.2% (n = 6) could provide the indication. The majority, or 96.3% (n = 26), were able to provide the dosage and administration instructions. In total, 44.4% (n = 12) stated that they read the instructions for the medications prescribed to them.

The average treatment knowledge score was 1.81 ± 0.74 , with score 2 (Good knowledge) being the majority in 55.6% (n = 15) of cases. All of our patients, 100% of cases, stated that they were satisfied with their treatment (**Table 4**).

Table 4. Distribution of patients according to treatment knowledge score.

Score	Effective	Percentage (%)
0	1	3.7
1	7	25.9
2	15	55.6
3	4	14.8
TOTAL	27	100

Regarding medication adherence, the mean MMAS-8 score reported in our patients was 4.78 ± 1.95 [range (1 - 8)]. Only 2 of our patients had a score of 8 (**Table 5**). Low adherence was reported more in patients who were on antimalarials with a frequency of 51.9%. Patients taking a combination of glucocorticoids and antimalarials were the least compliant in 29.6% (n = 8) of cases. Weariness, forgetfulness, fear of side effects and low socioeconomic level were the most reported factors by our patients in 51.9% (n = 14), 48.1% (n = 13), 40.7% (n = 11) and 29.6% (n = 8) of cases respectively (**Table 6**).

Table 5. Distribution of patients according to MMAS-8 score (Low adhesion < 6, Average membership 6-7, Strong adhesion = 8).

MMAS-8 Score	Effective	Percentage (%)
<1.17	1	3.7
[1.17 - 2.33[3	11.1
[2.33 - 3.50[3	11.1
[3.50 - 4.67[5	18.5
[4.67 - 5.83[6	22.2
[5.83 - 7[2	7.4
>7	7	25.9
TOTAL	27	100

Table 6. Distribution of patients according to factors linked to poor compliance.

Causes of non-compliance	Effective	Percentage (%)
Forgetfulness	13	48.1
Comorbidities	4	14.8
Low socioeconomic level	8	29.6
Availability	6	22.2
Side effects	11	40.7
High cost of products	4	14.8
Poly-medication	7	25
Weariness	14	51.9

Good knowledge of treatment was reported more in the age group over 36 years, but adherence was poor in this age group. Age over 36 years would be a factor that could negatively influence medication adherence (OR > 1), without a statistically significant relationship (P at 0.08). Poor knowledge was predominant among the uneducated. The level of education would be a factor that could negatively influence the degree of medication adherence (OR > 1), with a statistically significant relationship (P = 0.002) (**Table 7**). Prolonged duration of treatment would also be

a factor of poor treatment compliance in our patients (OR > 1), with a statistically significant link ($P < 0.05$).

Table 7. Distribution according to the correlation between education and the knowledge score.

Level of study	Perfect knowledge n (%)	Good knowledge n (%)	Poor knowledge n (%)	OR [95% CI]	P
Uneducated					
Yes	0 (0.00)	0 (0.00)	5 (71.42)	1.5 [1.1; 1.8]	0.02
No	5 (100)	15 (100)	2 (28.58)		
Primary					
Yes	0 (0.00)	1 (6.66)	1 (14.28)	1.2 [1.3; 2.2]	0.9
No	5 (100)	14 (93.33)	6 (85.72)		
Secondary					
Yes	4 (80)	4 (26.66)	1 (14.28)	1.1 [1.2; 2.3]	0.9
No	1 (20)	11 (73.34)	6 (85.72)		
Higher education					
Yes	1 (20)	10 (66.66)	0 (0.00)	1.7 [2.8; 3.6]	0.45
No	4 (80)	5 (33.33)	7 (100)		

4. Discussion/Comments

A total of 90 patients were identified. There were 63 patients who were not included in the study (57 patients were unreachable due to lack of telephone contact, 2 did not have a definitive diagnosis, 4 have a prolonged interruption of their treatment). We finally included 27 patients. This small number reduces the representativeness of the sample. It remains a preliminary study and must be supplemented by studies including larger cohorts.

This survey allowed us to see the level of knowledge and adherence to treatment among patients with SLE and/or RA followed in Niamey hospitals and to identify the difficulties and obstacles.

The mean age of our patients was 45.33 ± 15.55 years with extremes of 25 and 75 years. The age group over 36 years was the most represented with a frequency of 74.1% ($n = 20$). Our results are similar to those reported by Tinni A, Brah S and Andia A in Niger [5]-[7] on 2 studies on RA and one on lupus and corroborates the international literature. There is a clear female predominance among our patients, with a frequency of 92.60% ($n = 25$). These results are also comparable to those of Tinni A, Brah S and Andia A in Niger [5]-[7]. Our patients with a higher education level were the most represented with a frequency of 40.7% ($n = 11$). We

found 29.6% (n = 8) who were unemployed. Gadallah *et al.* in Egypt in 2015 had reported 79.2% of patients unemployed [11]. High blood pressure was the most found comorbidity with a frequency of 48.10% (n = 15) followed by diabetes with a frequency of 18.50% (n = 5).

Glucocorticoids are followed by antimalarials, and then immunosuppressants are the therapeutic classes used in 81.5% (n = 22), 66.7% (n = 18) and 40.7% (n = 11) respectively. Our results are similar to those reported by Oliveira-Santos *et al.* in Brazil in 2011 which had recovered respectively 80.08%, 69.51% and 47.15% [12]. On the other hand, in Zhang *et al.* study in China in 2017, the most used drugs were glucocorticoids (63.1%), nonsteroidal anti-inflammatory drugs (26.2%) and biological Disease-Modifying Anti-Rheumatic Drugs (b-DMARDs) (13.9%) [13].

In our study, prednisone and hydroxychloroquine were the most used molecules, 70.4% each, followed by methotrexate at 22.2%. Our result is superimposable with the data in the literature: Tinni A *et al.* in Niger in 2024 found respectively 90.90%, 43.43% and 67.67% [7]; Konan M *et al.* in Abidjan in 2021 reported 86.7%, 51%, 4.5% [14]; Yapa *et al.* in Bouaké (Cote d'Ivoire) in 2022 reported that corticosteroids were prescribed in 56% followed by hydroxychloroquine [15]; Gadallah *et al.* in Egypt in 2015 having reported respectively 85.7%, 91.4% and 75% [11]. After controlling for symptoms and inflammation, the two molecules used for cortisone sparing as the “gold standards” were hydroxychloroquine and methotrexate.

In our study, 67% (n = 18) of our patients were able to cite the names of their medications, 22.2% (n = 6) to give the indications, and 96.3% (n = 26) to give the dosage and methods of administration. Dhôte *et al.* reported in their study that age influenced knowledge of the indication but would influence knowledge of the name, according to Jaye *et al.* [16] [17].

In our study, the mean age of treatment duration was 8.33 ± 5.08 years [range (7 - 24)]. Our result is similar to that of Gu *et al.* in China in 2016, who reported a mean age of treatment duration of 8.76 ± 9.20 years [18]. The mean number of medications taken per patient is 2.11 ± 0.64 . The number between 3 - 5 predominated in 59.3% (n = 16). According to Oliveira-Santos and Zhang, the mean number of medications is 5.99 ± 2.48 and 4.16 ± 2.21 respectively [12] [13]. According to Kotry *et al.* [19]. As the number of drugs increased, they were less correctly identified by the patient, and similar results were reported by Hulka *et al.* [19] [20]. The average number of tablets taken daily by our patients was 2.33 ± 0.73 . There were 2 patients who took more than 8 tablets per day. Oliveira-Santos reported an average daily number of medications taken of 7.32 ± 4.48 [12].

Regarding the overall assessment of treatment adherence, low adherence was the most reported, followed by medium adherence and high adherence in 67% (n = 18), 26% (n = 7) and 7% (n = 2) respectively. Our results are comparable to those of Gadallah *et al.*, who reported 90.7%, 9.2% respectively and no patient obtained a high adherence score [11]. Chehab *et al.* in Germany in 2018 reported

4.8%, 32.5% and 62.7% respectively [21]. Some of our patients take more than 8 tablets per day; the quantity of tablets taken is certainly one of the causes of low adherence. The therapeutic strategy should limit the number of tablets to be taken as much as possible by adjusting the number of medications prescribed and, if possible, favoring fixed combinations.

Individual analysis of adherence to each therapeutic class showed that adherence to synthetic antimalarials is the lowest, followed by glucocorticoids and immunosuppressants in 51.9% (n = 14), 48.1% (n = 13) and 25.9% (n = 7) respectively. Our results are comparable to those of Koneru *et al.* in the USA in 2008 who reported that 51% of patients were not adherent to hydroxychloroquine and 39% to prednisone [22]. On the other hand, our results are different from those of Mazur-Nicorici *et al.* in Moldova in 2018 who reported high adherence to glucocorticoids followed by synthetic antimalarials and then immunosuppressants in 92.85%, 92.15% and 77.47% respectively [23]. We believe that better adherence to methotrexate, which is the immunosuppressant used, taken once a week, is more logical compared to hydroxychloroquine used every day in 2 doses!

SLE patients were the least compliant at 44.4% (n = 12). Our result is similar to those of Sun *et al.* in USA in 2022 who found 47% of SLE patients non-compliant [24]. Zhang *et al.* had reported better adherence in SLE patients (48.76%), followed by RA patients (38.57%) [13]. Gadallah *et al.* reported that 90.6% and 9.4% of RA patients were classified as low and moderately adherent respectively but none were classified as highly adherent to treatment [11]. Methotrexate is used predominantly in RA and taken once a week; it is also easier for a patient with RA to have better adherence compared to a lupus patient who takes hydroxychloroquine every day and in 2 doses.

The major barriers to treatment adherence reported by our patients were weariness, forgetfulness, fear of side effects and low socioeconomic level in 51.9% (n = 14), 48.1% (n = 13), 40.7% (n = 11) and 29.6% (n = 8) respectively. Our results are similar to those reported by Oliveira-Santos [12] *et al.* in Brazil. According to Garcia-Gonzalez *et al.*, the major reasons cited were lack of money to buy medications (52.38%), forgetfulness (38.21%), side effects (13.8%), interruption of treatment due to improvement of symptoms (7.72%) [25].

We assessed socio-economic status on the basis of patients' monthly income and whether or not they had health insurance. Obtaining health insurance remains a major challenge in Niger. Only 0.2% of the population reported having health insurance coverage in 2021 [9]. The government of Niger has initiated the process of setting up a mutual insurance scheme for public-sector employees which can facilitate access to medications used in these pathologies and improve compliance.

In the bivariate analysis, we noticed poor adherence to treatment in patients with low education levels (OR > 1, p = 0.02).

Lack of financial resources and low levels of education are factors often associated in Niger, which negatively impact medication adherence in the management

of all chronic pathologies in general and in the management of lupus and RA in particular. These factors have been reported in Congo regarding chronic diseases [8].

Furthermore, it should be noted that the workload of Niger doctors means that therapeutic education is not commonly carried out or is insufficient in the various clinical departments. In any case, a strategy to improve therapeutic compliance among patients must involve a good therapeutic education program.

5. Conclusion

The number of medications, the number of tablets, and the number of doses, among other factors, affect patient adherence to different treatments. It is important for physicians to adopt a prescription strategy that focuses on limiting themselves to the essentials, prioritizing single-dose molecules and, if necessary, fixed combinations. In Niger, the development of mutual health insurance planned by the government is an opportunity to improve access to medications and improve adherence. In all cases, therapeutic education must be well-developed among these patients. Further studies of larger cohorts are needed to better study compliance in these autoimmune diseases.

Conflicts of Interest

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

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