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Factors Associated with Non-Compliance among Patients with Chronic Kidney Disease at the Departmental University Hospital of Borgou and Alibori in Parakou (Benin)

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Abstract

Introduction: Therapeutic compliance in chronic kidney disease (CKD) represents a major challenge for the prevention of this condition, which is both a non-communicable disease (NCD) and a complication of other NCDs. Non-adherence to treatment (NOT) is a factor in the poor prognosis of CKD in developing countries, particularly in Benin. The aim of this study was to evaluate therapeutic compliance (TC) and determine the factors associated with non-compliance in patients with chronic kidney disease undergoing treatment at the Departmental University Hospital of Borgou and Alibori in Parakou (CHUD/B-A). **Patients and Methods:** This study was carried out in the Nephrology Department of CHUD/B-A. It was a cross-sectional, descriptive study with analytical aims that ran from December 25, 2022 to March 15, 2023 and covered data from 2017 to 2022. It involved 345 patient records meeting the diagnosis of CKD according to the KDIGO 2012 criteria. NOT was defined by a Girerd score evaluation greater than or equal to 3. Data processing and analysis were performed with R software version 4.3.0. **Results:** The mean age (SD) of patients was 50 years (±14.9). The prevalence of NOT was 57.1%. Potential predictors of non-adherence were: monthly revenue ($p = 0.009$), mode of admission ($p = 0.001$), phytotherapy ($p = 0.040$), traditional treatment ($p = 0.049$) and quantity of drugs ($p = 0.042$). **Conclusion:** Therapeutic compliance

among chronic kidney patients still needs to be improved through aware-ness-raising sessions.

Keywords

Chronic Kidney Disease, Therapeutic Non-Adherence, Girerd Assessment, Chronic Renal Failure, Benin

1. Introduction

Throughout the world, communicable diseases and epidemics that once accounted for the lion's share of the burden of morbidity and mortality are gradually giving way to chronic and degenerative diseases and accidents. The major public health burden lies in non-communicable diseases. Over the past two decades, mortality from communicable diseases has fallen, while mortality from non-communicable diseases (NCDs) has risen. In 2022, the World Health Organization (WHO) reported that non-communicable diseases (NCDs) were responsible for 74% of all deaths worldwide, with 17 million people dying each year from an NCD before the age of 70. Most of these deaths occurred in low- and middle-income countries [1] [2]. Chronic kidney disease (CKD) is one of the NCDs that are increasingly attracting the attention of the scientific community, particularly in Benin, where the burden of NCDs is on the rise. In the Nephrology Department of the National Hospital and University Center Hubert Koutoukou Maga (CNHU-HKM) in Cotonou, Benin, it accounted for 91% of admissions in 2018 [3]. One of the main challenges in preventing this condition is to ensure that patients maintain a good level of therapeutic compliance. Compliance with treatment in chronic patholo-gies fluctuates in the face of the multiplicity of alternative solutions. The pro-portion of chronically ill patients adhering to their treatment is only 50%, de-pending on the pathology [4]. Numerous studies have reported that an average of one-third of patients, with all pathologies combined, could be considered totally non-compliant [5]. In Africa, the standard of living in the face of benefit costs is an obstacle to therapeutic compliance in NCDs; the black race remains the least adherent to treatment [6]. In Benin, a study carried out in 2017 by Vigan *et al.* [7] at the CNHU-HKM in Cotonou showed that the prevalence of non-adherence to treatment was 48.67% among hemodialysis patients. The aim of our study was to evaluate therapeutic compliance and determine the factors associated with therapeutic non-compliance among chronic kidney patients at CHUD/B-A in 2022.

2. Materials and Methods

This descriptive cross-sectional study with analytical aims took place in the Neph-rology Department of the Departmental University Hospital of Borgou and Ali-bori in Benin from December 25, 2022 to March 15, 2023 and covered data from

2017 to 2022. These were patients diagnosed with chronic kidney disease according to the chronic kidney disease classification criteria [8] (KDIGO, 2012). Therapeutic compliance was assessed using the Girerd's scale at 6 months follow-up, with a threshold of poor compliance greater than or equal to 3.

The minimum expected sample size was determined using the Schwartz formula:

$$N = \frac{Z^2 pq}{i^2}$$

And this minimum size was determined from the prevalence of non-adherence reported by Vigan *et al.* (48.7%).

N = sample size of population.

p = prevalence of non-adherence of 89.2% reported in Benin by Vigan *et al.* [7] in 2017.

$q = (1 - p) = 10.8\%$.

$\alpha = 5\%$ (first-species risk) hence the value of the centered reduced deviation Z = 1.96.

$i = 0.06$, desired accuracy for results.

i.e. a minimum size of 267 chronic kidney disease.

All patient records meeting the following inclusion criteria were included in our study: any individual received during the study period, diagnosed with chronic kidney disease according to KDIGO 2012 criteria whatever the stage of the disease, followed up for at least 6 months with regular assessment of Therapeutic compliance according to the Girerd's scale [9]. Incomplete and unusable chronic kidney disease files were excluded (6 chronic kidney disease).

2.1. Study Variables

- **The dependent variable** was non-adherence to therapy assessed using the Girerd's scale [9].
- **The independent variables were:**
  ○ Socio-demographic and economic characteristics: Age, sex, professional status, marital status, income, distance travelled.
  ○ Clinical data: Time of consultation, previous treatment, reason for consultation, mode of admission, general condition, blood pressure, heart rate, stages of chronic kidney disease, heart rate.
  ○ Therapeutic data: Quantity of medications.
- **Operational definitions of variables were:**
  ○ CKD was diagnosed according to the classification criteria for chronic kidney disease [8] (KDIGO, 2012). Stages 2, 3, 4 and 5 were retained for a glomerular filtration rate (GFR) between 60 and 89 ml/min/1.73 m^2, 30 and 59 ml/min/1.73 m^2, 15 and 29 ml/min/1.73m^2 and less than 15 ml/min/1.73 m^2 respectively.
  ○ The chronic kidney disease epidemiology collaboration (CKD-EPI) equation was used as the basis for calculating GFR [8].
  ○ Past treatment was the type of treatment used prior to the consultation

which could be phytotherapy when it is the practice of phytotherapy; traditional when it is the use of a traditional healer who uses rituals and invokes spirits to heal the patient. This later treatment can be accompanied by phytotherapy and medication when instituted by a health professional;

○ The consultation delay is the time elapsed between the onset of symptoms and the first contact with health services.

○ Blood pressure was measured in a seated subject after 15 minutes of rest, using an automatic digital blood pressure monitor fitted with a cuff (belonging to the list of blood pressure monitors validated by the French Society of Hypertension). It was taken on the bare right arm, and placed on a table with the palm facing upwards. Three measurements were taken at five-minute intervals; the average of the last two measurements was the blood pressure retained for each patient. Blood pressure is considered high when it is greater than or equal to 140/90 mmHg [10].

○ Heart rate (HR) was considered normal for a number of heartbeats between 60 and 100 beats (bpm) per minute. It was taken 15 minutes after the patient's arrival, on the bare right arm, placed on a table, palm upwards, with the same automatic digital blood pressure meter fitted with a cuff used for blood pressure measurement.

○ The Girerd's [9] scale is used to determine therapeutic non-adherence. The items on Girerd's [9] scale are: forgetting to take medication, running out of medication, delay in taking medication, amnestic stroke, feeling that treatment is doing more harm than good, and feeling that there are too many pills to take. It is validated in a patient when the number of affirmative responses is greater than or equal to 3. A total of 0 indicates good compliance. A total of 1 or 2 indicates a minimal compliance problem, and a total of 3 or more indicates poor compliance. In this study, the first two modalities (good compliance and minimal problem) were categorized as good compliance and the last one (poor compliance) as non-compliance.

○ The number of medications was the amount of oral medication patients were taking on the day of the adherence assessment.

2.2. Data Collection and Analysis

Data were collected using a medical record tabulation form, covering patients' socio-demographic, economic, clinical and therapeutic variables. Data were analyzed using R 4.3.0 software. Quantitative variables were expressed as means with standard deviations, and qualitative variables as proportions. Chi^2 and Fisher tests were used to determine the association between two qualitative variables. Student's T-test was used to compare means. A statistically significant association was established for a p-value < 0.05. The variables associated with the univariate analysis were introduced into the multivariate analysis model. Potential predictor variables were identified from binary logistic regression analysis, with odds ratios (OR) and their 95% confidence intervals (95% CI) determined.

2.3. Ethical Considerations

The survey protocol was validated by the Public health unit of the Cotonou Faculty of Health Sciences. Collection authorizations were obtained from the aforementioned unit and from the Head of the CHUD/B-A Nephrology Department. The anonymity and confidentiality of the data collected complied with the ethical principles applicable to medical research on human subjects contained in the Declaration of the World Medical Association of Helsinki.

3. Results

From January 1, 2017 to December 31, 2022, a total of 621 new patients were received in the CHUD/B-A Nephrology Department, including 345 cases of chronic kidney disease. Of the 345 cases of chronic kidney disease, 148 had good compliance and 197 had poor compliance.

3.1. Socio-Demographic Characteristics

The mean age of patients was 50 ± 14.9 years (CI 95% [48.4 - 51.6]), with extremes of 13 and 90 years. Patients aged between 40 and 60 were the most numerous (47.2%). Over half the patients (66.7%) were male, giving a sex ratio (M/F) of 2. The majority (36.8%) had no formal education. In terms of monthly income, 163 patients (47.2%) had monthly revenue of between 52,000 - 150,000 FCFA, most of them having come from less than 50 km away (61.7%) (Table 1).

3.2. Clinical and Therapeutic Characteristics of Patients

Some 275 patients, or 79.7% of the total, were admitted with an altered general condition. According to the mode of admission to the department, 65.5% of patients were referred by consultants, the majority of whom (69.9%) were general practitioners. More than half of patients (71.6%) came for consultation at stage 5 of the disease. More than three-quarters (85.5%) of patients had received prior treatment before consulting the nephrology department. Of these, 65.2% had opted for a previous herbal treatment (phytotherapy). All patients (100%) received therapeutic education prior to treatment. The average number of oral medications taken by patients was 4.3 ± 1.7, with extremes of 2 and 9 molecules. Most patients were on 4 molecules. The average number of molecules differed statistically (p = 0.004) between the group of patients with good compliance (4.6 ± 1.7) and those with poor compliance (4.1 ± 1.7) (Table 2).

3.3. Prevalence of Non-Compliance

Evaluation of the various items on the Girerd's scale showed that 60.6% of patients were late in taking their medication in relation to the usual times, and 58% mentioned medication breakdowns. The evaluation of therapeutic compliance showed that 197 patients were noncompliant, giving a prevalence of non-compliance equal to 57.1% (Figure 1, Table 3).

Table 1. Distribution of patients by socio-demographic and economic characteristics, CHUD/B-A 2017-2022.

	Frequency (n = 345)	Percentage
Age range (year)		
[0 – 21[	7	2.1
[21 – 41[	93	26.9
[41 – 61[	163	47.2
[61 – 81[	75	21.7
>81	7	2.1
Gender		
Male	230	66.7
Female	115	33.3
Marital status		
Unmarried	32	9.3
Married	313	90.7
Monthly revenue (FCFA)[a]		
<52,000	72	20.9
52,000 - 150,000	163	47.2
150,000 - 300,000	84	24.4
>300,000	26	7.5
Study level		
No schooling	127	36.8
Primary level	62	17.9
Secondary level	79	22.9
Higher education	77	22.4
Professional status		
Employed	234	67.8
Unemployed	61	17.7
Retired	50	14.5
Residence environment		
Urban	230	66.67
Rural	115	33.33
Distance travelled (km)		
≤50	213	61.7
>50	132	38.3

[a]1 FCFA = 0.0016$.

Table 2. Patient distribution by clinical and therapeutic characteristics, CHUD/B-A 2017-2022.

	Frequency (n = 345)	Percentage
Consultation delay (day)		
≤7	6	1.7
[8 – 91[	162	46.9
[91 – 181[	68	19.8
≥181	109	31.6
General clinical condition		
Good	70	20.3
Altered	275	79.7
Admission mode		
Direct	119	34.5
Referred	226	65.5
Heart rate		
Normal	219	64.3
High	112	32.6
Low	14	4.1
Blood pressure (BP)		
Normal	81	23.5
High	261	76.5
Past treatment		
Medicinal	244	65.2
Phytotherapy	74	19.8
Traditional	56	15.0
Quantity of drugs		
≤5	261	75.6
>5	84	24.4

Table 3. Evaluation of therapeutic non-adherence according to Girerd, CHUD/B-A 2017-2022.

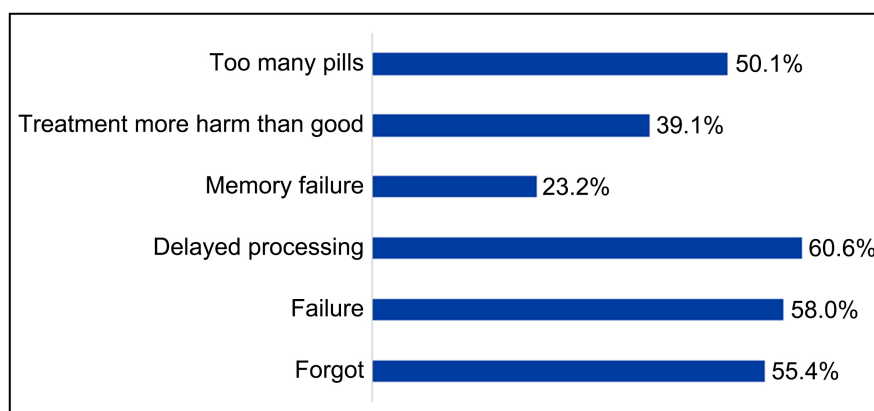|	Frequency (n = 345)	Percentage
Good compliance	58	16.8
Minimal compliance problems	90	26.1
Bad compliance	197	57.1

Figure 1. Classification of therapeutic adherence according to the Girerd's scale, CHUD/B-A 2017-2022.

3.4. Factors Associated with Non-Compliance

3.4.1. Socio-Demographic and Economic Characteristics

Only two variables had a statistically significant relationship with compliance: monthly income (p = 0.005) and distance travelled (p = 0.01). Patients with a monthly income of more than 300,000 FCFA had an 80% lower risk of poor compliance than patients with an income of less than 52,000 FCFA. Patients from more than 50 km away were 1.8 times less compliant than patients from less than 50 km away. Other characteristics were not associated with compliance at the 5% level (Table 4).

3.4.2. Clinical and Therapeutic Characteristics

Among clinical and therapeutic characteristics, there was a statistically significant relationship between therapeutic compliance and mode of admission (p = 0.012), herbal medicine as previous treatment (p = 0.000), previous traditional treatment (p = 0.006), previous drug-based treatment (p = 0.005) and the number of tablets the patient took orally (p = 0.023).

Referred patients were 1.8 times less compliant than self-referred patients. The risk of poor compliance was reduced by 70% in patients who had opted for phytotherapy prior to consultation, and by 80% in patients who had opted for traditional treatment (80%) prior to consultation. Patients who opted for self-medication and/or a prescription from a healthcare professional were 2 times less compliant. As for the number of oral medications taken, the risk of poor compliance was reduced by 40% in patients taking more than 5 tablets (MRC and adjuvant treatments) (Table 5).

Multivariate analysis showed that the potential predictors of poor compliance in the Nephrology Department of CHUD/B-A in 2023 were monthly income (p = 0.009), phytotherapy (p = 0.004), traditional treatment (p = 0.045), mode of admission (p = 0.001) and number of tablets (p = 0.0042). Low monthly income and referral were risk factors for poor compliance, whereas previous phytotherapy and traditional treatment, and number of oral tablets above 5, were protective factors against poor compliance.

Table 4. Relationship between patient compliance and socio-demographic and economic characteristics, CHUD/B-A 2017-2022.

	Therapeutic compliance			
	Good n (%)	Poor n (%)	OR (95%)	p
Age range (year)				0.879
[0 – 21[	4 (2.7)	3 (1.5)	1	
[21 – 41[	41 (27.7)	52 (26.4)	1.7 (0.3 - 7.9)	0.507
[41 – 61[	71 (47.9)	92 (46.7)	163 (47.4)	0.483
[61 – 81[	29 (19.6)	46 (23.4)	75 (21.7)	0.349
>81	3 (2.1)	4 (2.0)	7 (2.0)	0.594
Gender				
Male	98 (66.2)	132 (67.0)	1	
Female	50 (33.8)	65 (33.0)	0.96 (0.6 - 1.5)	0.878
Marital status				
Unmarried	15 (10.1)	17 (8.6)	0.8 (0.4 - 1.7)	0.634
Married	133 (89.9)	180 (91.4)	1	
Study level				0.294
No schooling	49 (33.1)	78 (39.6)	1	
Primary level	25 (16.9)	37 (18.8)	0.9 (0.5 - 1.7)	0.818
Secondary level	41 (27.7)	38 (19.3)	0. 7 (0.3 - 1.03)	0.062
Higher education	33 (22.3)	44 (22.3)	0.8(0.5 - 1.5)	0.546
Monthly revenue (FCFA)[a]				**0.001**
<52,000	31 (20.9)	41 (20.8)	1	
52,000 - 150,000	55 (37.2)	108 (54.8)	1.5 (0.8 - 2.6)	0.173
150,000 - 300,000	42 (28.4)	42 (21.3)	0.7 (0.4 - 1.4)	0.387
>300,000	20 (13.5)	6 (3.1)	0.2 (0.08 - 0.6)	**0.005**
Distance travelled (km)				
≤50	103 (69.6)	110 (55.8)	1	
>50	45 (30.4)	87 (44.2)	1.8 (1.2 - 2.8)	**0.010**

[a]1 FCFA = 0.0016$.

Table 5. Relationship between patient compliance and clinical and therapeutic characteristics, CHUD/B-A 2017-2022.

	Therapeutic compliance			
	Good n (%)	Poor n (%)	Total	p
General clinical condition				
Good	26 (17.57)	44 (22.34)	1	
Altered	122 (82.43)	153 (77.66)	0.3 (0.2 - 0.5)	0.278
Admission mode				
Direct	62 (41.9)	57 (28.9)	1	
Referred	86 (58.1)	140 (71.1)	1.8 (1.1 - 2.7)	**0.012**
Stage of CKD				**0.043**
Stage 2	0 (0.00)	2 (1.0)	1	
Stage 3	15 (10.1)	21 (10.7)	0.0 (0.0-)	0.99
Stage 4	16 (10.8)	44 (22.3)	0.0 (0.0-)	0.99
Stage 5	117 (79.1)	130 (66.0)	0.0 (0.0-)	0.99
Phytotherapy (past treatment)				
No	98 (66.2)	173 (87.8)	1	
Yes	50 (33.8)	24 (15.2)	0.3 (0.2 - 0.5)	**<0.0001**
Traditional (past treatment)				
No	108 (72.9)	181 (91.9)	1	
Yes	40 (27.1)	16 (8.1)	0.2 (0.1 - 0.4)	**0.006**
Medical (past treatment)				
No	55 (37.2)	46 (23.4)	1	
Yes	93 (62.8)	151 (76.6)	1.9 (1.2 - 3.1)	**0.005**
Number of drugs				
≤5	102 (68.9)	159 (80.7)	1	
>5	46 (31.1)	38 (19.3)	0.6 (0.3 - 0.9)	**0.023**

Patients with a monthly revenue of less than 52,000 FCFA and between 52,000 - 150,000 FCFA had respective risks of non-compliance of 3.7 [1.2 - 11.7] and 5.0 [1.8 - 14.2] compared with patients with an income of over 300,000 FCFA. Referred patients had 2.3 [1.4 - 3.7] times the risk of non-adherence compared with those who came directly for consultation. Previous herbal and traditional treatments and a high number of drugs were protective factors. They protected patients against non-compliance by 50%, 60% and 40% respectively, compared with those who had not taken any prior treatment (Table 6).

Table 6. Multivariate model of potential predictors of CKD non-compliance at CHUD/B-A in 2022, CHUD/B-A 2017-2022.

	Non-compliance with medication				
	Total (N)	NCT[a] (n)	% (n/N)	OR[b] (IC 95%)	p
Monthly revenue (FCFA)[c]					**0.009**
<52,000	72	41	56.9	3.4 [1.2 - 10.3]	**0.025**
52,000 - 150,000	163	108	66.2	4.8 [1.7 - 13.6]	**0.003**
150,000 - 300,000	84	42	50.0	2.3 [0.9 - 7.3]	0.096
>300,000	26	6	23.1	1	
Phytotherapy (past treatment)					
No	271	173	63.8	1	
Yes	74	24	32.4	0.5 [0.2 - 0.9]	**0.040**
Traditional (past treatment)					
No	289	181	62.6	1	
Yes	56	16	28.6	0.4 [0.2 - 0.9]	**0.049**
Admission mode					
Direct	119	57	47.9	1	
Referred	226	140	61.9	2.3 [1.4 - 3.7]	**0.001**
Number of drugs					
≤5	261	159	60.9	1	
>5	84	38	45.2	0.6 [0.3 - 0.9]	**0.042**

Binary logistic regression: 1 is for the reference/comparison modality; [a]Non-compliance with treatment; OR[b]: adjusted odds ratio; [c]1 FCFA = 0.0016$.

4. Discussion

4.1. Prevalence of Non-Compliance

The prevalence of therapeutic non-adherence was 57.1% at CHUD/B-A in 2022. This result is similar to the one of Yousfi *et al.* [11] in Tunisia in 2012, who reported prevalences ranging from 20% to 60% and depending on the number of medications taken per day. Similarly, Bettaieb *et al.* [12], measuring therapeutic compliance in chronic hemodialysis patients in Tunisia, and Vigan *et al.* [7] in Cotonou reported prevalences of 57.35% and 48.67% respectively. However, our result was lower than the 89.2% found in Togo by Sabi *et al.* [13] and higher than the 10.4% reported by Parmier *et al.* [14] in France in 2012.

4.2. Factors Associated with Patient Compliance

In our study, the factors associated with NOT in CKD patients were: income, mode of admission, number of drugs, and previous treatment with herbs or traditional healers. Our results are similar to those of Seck *et al.* [15], who reported that factors contributing to poor compliance included adverse drug reactions and high drug costs.

4.2.1. Monthly Income and Treatment Accessibility

Patients with a monthly income of less than 52,000 FCFA and between 52,000 - 150,000 FCFA were respectively 3.7 times and 5 times more likely to be non-compliant with treatment than patients with an income of over 300,000 FCFA. This may be explained by the difficulty of meeting the direct and indirect costs of treatment for patients with modest incomes. Financial capacity affects the entire treatment process: consultation, complementary examinations, purchase of medication, compliance with follow-up appointments, logistics, etc. Income thus determines therapeutic compliance, as reported in a study by Higuchi [16] on access to care for the treatment of chronic diseases in low- and middle-income countries. The author identified high medical costs as a direct consequence of poor compliance with treatment.

4.2.2. Admission Mode

Referred patients were 2.3 times more likely to be non-compliant than those admitted directly. This finding can be explained by several factors. Firstly, voluntary request for care in a specialized nephrology department through direct admission, usually after failure of other therapies, is a sign of patient awareness and action. On the other hand, admission on referral, after referral by a healthcare professional and a richly nourished awareness campaign, may signal for the patient the hope of a cure, which is quickly stifled by the true and sometimes alarming therapeutic education delivered for chronic kidney patients. Finally, it is important to question the quality of the information provided upstream of the referral, and the multidisciplinary collaboration offered to patients who now have to deal with several medical expenses simultaneously. It is likely that overlapping appointments and the high cost of treatment by several specialists are at the root of therapeutic non-compliance. The distance travelled by referred patients could also be a factor in non-adherence, given the cost of transport; bearing in mind that most referred patients lived in rural areas.

4.2.3. Past Treatments

Phytotherapy and traditional treatment as previous therapies were protective factors against non-adherence. This could be explained either by patients' awareness of the failure of these practices in response to the symptoms of chronic kidney disease, or by a feeling of invulnerability acquired as a result of these treatments, which would henceforth authorize the patient to resort more serenely to so-called more modern therapies. Added to all this is the fear of dialysis at the

final stage of the disease evolution, which could raise the patient's awareness and improve compliance. Therapeutic education carried out at each check-up by healthcare staff as part of their follow-up of patients with CKD could be an important element in the return to good therapeutic compliance. As such, this result could signify the success of awareness-raising messages shared within the department.

4.2.4. Number of Drugs in the Patient Treatment Regimen

According to the results of our study, a high number of molecules protects against non-adherence to therapy, and thus improves compliance. Each additional molecule in a patient's regimen represents an additional disorder or dysfunction to be corrected. This could have a deterrent effect on patients, especially in view of the therapeutic education they receive. As the kidneys are involved in the elimination of patients, those already suffering from CKD are at risk of progressing to the terminal stage, with the possibility of treatment by hemodialysis. What's more, adjuvant molecules or those prescribed in response to symptoms improve clinical conditions and give patients renewed hope, making them even more compliant. Family pressure and support, linked to the fear aroused by the large quantity of drugs to be used, could also explain this result. Family and friends would see this as a worsening of the patient's condition, requiring more rigorous monitoring of medication intake to avoid complications or even premature death.

4.3. Limitations of Study

Our study did not enable us to assess compliance with treatment in terms of follow-up appointments, prescription and paraclinical test renewals, hygienic and dietary measures, psychosocial aspects or quality of life. For a chronic disease with long-term treatment, the evaluation of these parameters could provide a holistic assessment of the handicaps to therapeutic compliance. A qualitative assessment of the reasons for poor compliance was also lacking.

5. Conclusion

Non-adherence to treatment is a major problem among patients with chronic kidney disease at CHUD/B-A while referred patients with low incomes were less compliant. From diagnosis to treatment, including the mode of admission, communication and therapeutic education were essential for good treatment compliance. So, adherence to treatment can be improved if work is carried out at the time of diagnosis, before referral and at the time of treatment initiation. Hence, the raising of awareness could be more developed among patients and those around them about the benefits of good treatment compliance and keeping follow-up appointments.

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Authors' Contributions

All authors have contributed to the correction of the document.

Conflicts of Interest

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

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