

Factors of Non-adherence to Antidiabetic Drugs in Type 2 Diabetics, Antananarivo Madagascar

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Abstract: *Introduction:* The non-adherence to therapy of diabetics is grafted with heavy morbidity and mortality. Our study aims to determine the factors of non-adherence with antidiabetic drugs in type 2 diabetics. *Methods:* This was a descriptive and analytical cross-sectional study, carried out in the Endocrinology Unit of the Joseph Raseta University Hospital Center. Befelatanana, Antananarivo, over a period of 7 months. Adherence to treatment was assessed by the Morisky scale. *Results:* We retained 104 patients with an average age of 58.36 years, consisting of 52.88% of women. Adherence was high, medium, and low in 6.73%, 31.73% and 61.54% of cases, respectively. From their attending physician, explanations of the diabetic disease and their treatment were received by 90.38% and 66.35% of patients, respectively. However, these patients were aware of their disease and treatment in 18.27% and 41.35% of cases, respectively. The most observed non-adherence factors were the absence of an appointment given by the physician (30.77%), the feeling of well-being (24.04%), the lack of money (21.15%), forgetting (20.19%) and advice from a traditional practitioner (16.35%). Only the doctor's explanation for diabetes treatment was significantly associated with medication nonadherence ($p=0.0310$). *Conclusion:* Continuing medical education for physician is essential so that they can strengthen therapeutic education and follow-up for their diabetics.

Keywords: Antidiabetic Drugs, Diabetes Mellitus, Madagascar, Morisky Score, Non-adherence

1. Introduction

Globally, diabetes mellitus is one of the leading causes of cardiovascular mortality. Its prevalence is steadily increasing in both developed and developing countries [1]. It is a chronic disease that requires strict long-term management and monitoring. One of the problems with this management concerns above all therapeutic adherences. The latter constitutes one of the cornerstones of the therapeutic success of the disease and non-compliance thus leads to severe morbidity and mortality.

According to the World Health Organization (WHO), medication adherence is "the extent to which the behaviors of a person having to take a drug, follow a diet and / or change

their lifestyle corresponding to the recommendations agreed with a health professional". In other words, it corresponds to a degree of fit between the behavior and a medical prescription or recommendation [2].

Only 50% of patients with chronic disease would be truly observant. This figure would be even lower in developing countries [2]. Diabetes mellitus is a difficult disease to manage successfully as the rate of non-compliance has been reported to be extremely high [3]. In Africa, the rate of low adherence to therapy in diabetics ranged from 32.5% to 55% [4-6].

In Madagascar, truly little data is available from the study on treatment adherence in diabetic patients. The objectives of our study are to assess adherence and factors of non-adherence to antidiabetic drugs in patients with type 2

diabetes, to propose intervention planning to overcome barriers.

2. Methods

We carried out a cross-sectional study with a descriptive and analytical aim. It took place in the Endocrinology Care, Training and Research Unit of the Joseph Raseta Befelatanana University Hospital Center in Antananarivo, Madagascar, for a period of four months (from September 1 to December 31, 2018).

To be included in the study, the patients should have been known to have type 2 diabetes for at least 6 months and had previously benefited from a follow-up consultation at the said study site. Diabetes diagnosis and typing were made according to the criteria of the American Diabetes Association [7]. Patients who refused to participate and were unable to complete the questionnaire were excluded from the study.

The parameters studied were the gender and age of the patients, the duration of the development of diabetes, the circumstances of discovery of diabetes, the antidiabetic drugs taken, the chronic diseases associated with diabetes, the number of drugs taken, the frequency of follow-up diabetes, the monthly cost of medication, obtaining explanations about diabetes and their diabetes treatment from their attending physician, patients' knowledge of diabetes and their antidiabetic treatment, adherence measured using the Morisky scale [8] and the factors of non-adherence with treatment.

Data were collected using a pre-tested and validated questionnaire. Statistical analysis was performed using Epi-infoTM software version 3.5.4. The results are represented in absolute value, in percentage and in average. We used Pearson's Chi-Square Test to test for correlation with significance level p value < 0.05.

3. Results

During the study period, we selected a total of 104 patients with type 2 diabetes who met the eligibility criteria.

Table 1 presents the general characteristics of our study population. It was made up of 49 men and 55 women giving a sex ratio of 0.89. Their mean age was 58.36 ± 11.34 years with extremes of 33 years and 94 years. Their diabetes had a mean duration of 5.01 ± 4.83 years, was diagnosed during routine screening, and is currently treated with regular insulin in 68.27% and 63.46% of cases, respectively. More than four out of five patients had at least one monthly follow-up for their diabetes. High blood pressure was the most common associated chronic disease. Half of the patients were taking 4 to 6 drugs per day. Note that these drugs included both antidiabetics and the treatment of co-morbidities.

Regarding the patient- physician relationship, only 9.62% of patients had not received an explanation from the physician about the diabetic disease and 33.65% about the treatment of diabetes. However, 73.08% of them said they had no diabetes at all and 58.65% their treatment. In addition, only one in four

patients recognized that the duration of diabetes treatment is lifelong (Figure 1).

Figure 2 showed the levels of medication adherence according to the Morisky scale. Sixty-one-point fifty-four percent of the patients were poor observers. The factors for their non-compliance were multiple; the lack of an appointment given by the physician had held the first place (Table 2).

Table 1. General characteristics of the study population (N=104).

Variables	Number of cases (%)
Gender	
Male	49 (47.12)
Female	55 (52.88)
Age group (years)	
[33 – 50]	26 (25.00)
[50 – 70]	67 (64.42)
[70 – 94]	11 (10.58)
Duration of diabetes (years)	
[0.5 – 5]	49 (47.11)
[5 – 10]	31 (29.81)
[10 – 23]	24 (23.08)
Circumstances of discovery of diabetes	
Systematic screening	72 (69.23)
Complications of diabetes	29 (27.89)
Systematic screening and complications of diabetes	2 (1.92)
Cardinal syndrome	1 (0.96)
Antidiabetic drugs taken *	
Regular insulin	66 (63.46)
Insulin mix	25 (24.04)
Glibenclamide	33 (31.73)
Metformin	5 (4.81)
Glimepiride	1 (0.96)
Gliclazide	1 (0.96)
Diabetes follow-up frequency (months)	
[1 - 3]	84 (80.77)
[3 - 6]	15 (14.42)
[6 - 12]	4 (3.85)
[12 -	1 (0.96)
Chronic diseases associated with diabetes.	
Any	51 (49.04)
Arterial hypertension	50 (48.08)
Other**	3 (2.88)
Number of drugs taken per day.	
1 to 3	37 (35.58)
4 to 6	52 (50.00)
7 to 9	15 (14.42)

* Patients might take one or more classes of anti-diabetic drugs.

** Other associated chronic diseases were asthma, chronic obstructive pulmonary disease, and gout.

After univariate analysis, only the explanation of the treatment of diabetes by the attending physician was significantly associated with nonadherence to medication ($p=0.0310$). Table 3 presents the entire statistical analysis between the Morisky scale and the different variables.

4. Discussion

Adherence to therapy should be assessed throughout treatment, either directly or indirectly. Among the indirect measurement methods, the first self-administered

questionnaire developed in 1986 by Morisky, Green, and Levine consisted of only 4 questions dealing with voluntary forgetting and not taking medication. It then evolved in 2008 and then consisted of 8 questions, the 4 questions are supplemented by other questions relating more to the patient's feelings [8-10].

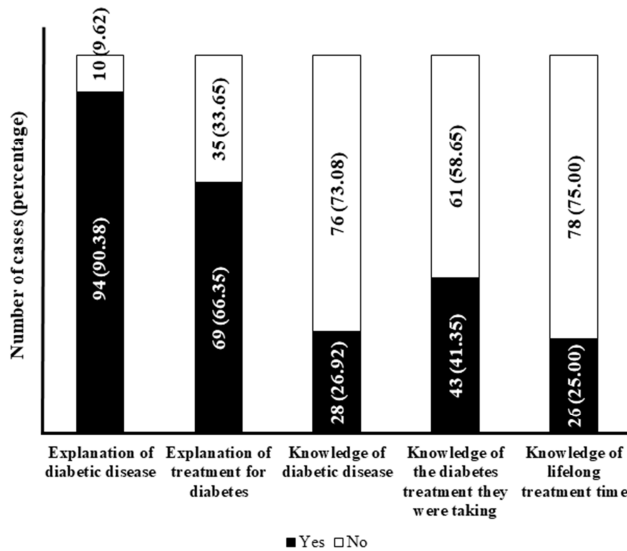


Figure 1. Distribution of patients according to the explanations received from the physician and their knowledge (N=104).

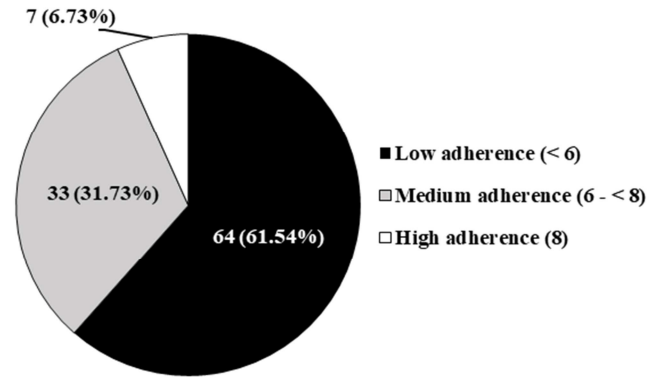


Figure 2. Distribution of patients according to Morisky score (N=104).

The female predominance (sex ratio=0.89) that we found in our study matched that of Alwan et al (sex ratio=0.66) [11]. However, Mukherjee et al in India had found a male predominance (sex ratio=1.97) [12]. We did not find a significant correlation between gender and treatment adherence in our study. However, the non-compliance of men (69.34%) was greater than that of women (65.45%) (p=0.003) in another study [13]. Indeed, in the DIABASIS study, women took the disease more seriously and participated more in self-management, while men relied more on family support [14]. Thus, physicians should take these gender differences in attitude into account when counseling, educating, and treating patients.

Table 2. Distribution of patients according to factors of non-adherence (N=104).

Factors of non-adherence*	Number of cases (%)
No appointment given by the physician	32 (33.77)
Feeling of well-being	25 (24.04)
Lack of money	22 (21.15)
Oversight	21 (20.19)
Advice from a traditional practitioner	17 (16.35)
Prescription not renewed by the doctor	11 (10.58)
Physician or health center too far away	10 (9.62)
Lack of confidence in treatment	8 (7.69)
Out of stock at the pharmacy	7 (6.73)
Professional occupation	7 (6.73)
Advice from the entourage	6 (5.77)
Occurrence of side effects	4 (3.85)
Other**	3 (2.88)
Religious belief	2 (1.92)

* Each patient surveyed was entitled to three different reasons for stopping treatment.

** Others: patient's decision, complexity of the treatment, depression.

Table 3. Statistical analysis between the Morisky score and the different variables.

Variables	Morisky Scale			p value
	Adherence			
	High	Medium	Low	
Gender				
Male	2	14	33	0.4136
Female	5	19	31	
Age group (years)				
[33 – 50]	0	8	18	0.5375
[50 – 70]	6	22	39	
[70 – 94]	1	3	7	
Duration of diabetes (years)				
[0.5 – 5]	4	17	27	0.3135
[5 – 10]	2	7	22	

Variables	Morisky Scale			p value
	Adherence			
	High	Medium	Low	
[10 – 23]	1	8	15	0.2645
Number of drugs taken per day.				
1 to 3	3	9	24	
4 to 6	3	21	37	
7 to 9	1	3	3	0.9092
Explanations received from the doctor on:				
Diabetic disease				
Yes	6	30	58	
No	1	3	6	0.0310
Antidiabetic treatment				
Yes	7	25	37	
No	0	8	27	
Patient knowledge about:				0,9357
Diabetic disease				
Yes	2	9	17	
No	5	24	47	
Antidiabetic treatment				0.5215
Yes	2	16	25	
No	5	17	39	

In our study, the mean age of patients was 58.36 years. This was like that of the study by Khotkar et al, whose average age of their population was 54 years [15]. On the other hand, in France the mean age of the population of Tiv et al was 65 years [16]. This difference in the average age of the populations studied could be explained by the aging of the population of European countries including France.

Among our patients, 47.11% had diabetes progressing for less than 5 years, 29.81% for 5 to 10 years and 23.08% for more than 10 years. This finding was similar to that of the study in India, where 46.17% of their patients had diabetes for less than 5 years and 53.83% had diabetes for 5 years and more [12]. This was a little different from that of Bruce et al with 47.5% of patients diagnosed for 5 to 10 years, 31% less than 5 years and 18% more than 10 years [17]. In our series, we did not find a significant association between the duration of diabetes progression and treatment adherence ($p=0.3135$). However, some authors had found that a prolonged duration of diabetes was associated with non-compliance with treatment [18]. Thus, therapeutic education should be repeated at each medical consultation, even for the oldest diabetics.

In 68.27% of cases, diabetes was discovered by mass screening and in 27.88%, at the stage of complications. However, in a study conducted in France, diabetes was diagnosed during a systematic examination in 73% of cases [19]. This high rate of diabetes, which was already complicated in our study, could be due to the insidious nature of type 2 diabetes which is the cause of the frequency of delayed diagnosis.

In our study, patients might be taking one or more classes of anti-diabetic drugs. Insulin was prescribed more than oral antidiabetics (87.50% vs. 38.46%). On the other hand, Elsous et al had reported that only 23% of their patients were on insulin therapy [20]. This could be explained by the fact that our study was carried out in a hospital center. In fact, diabetes was most often complicated, and / or in major imbalance, and / or associated with an intercurrent condition requiring transient

or even definitive insulin therapy. Moreover, in Madagascar we only have metformin, sulfonamides, and gliptins as ADO.

The frequency of diabetes follow-up was closer in our series with a monthly follow-up rate of 80.77%. This could be explained by the fact that our patients generally came in consultation with their attending physician to have their capillary blood sugar checked, because most of them did not have a glucometer. In addition, almost all our patients (87.5%) were on insulin.

Hypertension remains the most common chronic disease associated with diabetes in our series as in other studies [20]. Particularly in type 2 diabetics, insulin resistance and reactive hyperinsulinemia contribute to the onset of hypertension, through sodium retention and imbalance between sympathetic activation and lack of vasodilation [21].

In combination with the treatment of co-morbidities, half of our patients were taking 4-6 drugs per day. In a study in Virginia, 48.1% were on diabetes monotherapy; 43.8% on dual therapy and 7.6% on triple therapy [22]. Despite the lack of correlation between the number of drugs taken and adherence in our study, some authors had shown that the adherence rate decreased as the number of drugs increased [23].

Among our patients, 90.38% had received an explanation about diabetes from their physician, which was consistent with those in the literature where each patient had received an explanation of diabetes, regarding the signs and complications so that the treatment is well followed [24]. Despite this, the rate of ignorance of diabetes by our patients was high (73.08%) as in the literature [25]. This could be explained by the fact that the patients were either unable to understand the physician's explanation, or the latter had not been able to explain to the patients well, or both situations at the same time. This already implies the importance of repeating therapeutic education at each consultation.

In the present study, on the one hand, 66.35% of patients had received an explanation for the treatment of their diabetes.

On the other hand, only one in four patients said they knew about their treatment. However, obtaining an explanation of the treatment by the patient is significantly correlated with treatment compliance ($p=0.031$).

According to the Morisky scale, 6.73% of our patients had high adherence, 31.73% medium adherence and 61.54% low adherence. Using the same evaluation method, Sajith et al found that their patients' treatment adherence levels were high for 40.95% of patients, medium for 37.14% and low for 21.91% [26]. In Uganda, James et al had considered their patients who had taken 80% or more of the prescribed doses in the last seven days to be adherent to antidiabetic drugs. At the end, the rate of adherent patients was 83.3% [27]. These differences in the level of compliance could be explained by the diversity of the populations studied with all environmental factors and socio-economic status, but also by the methods used to assess therapeutic adherence.

In our study, the absence of an appointment given by the physician was the most objectified factor of non-adherence (30.8%), followed by the feeling of well-being (24%), the lack of money (21.2%) and forgetting (20.2%).

Heissam et al showed that 53.46% of participants sometimes forgot to take medication and 43.09% of participants sometimes stopped taking their medication when they felt well [28]. According to Shuvankar et al. in India, forgetting was the leading cause of medication non-adherence in 44.7% of cases, followed by the high cost of diabetes medication in 32.7% of cases and feelings of well-being and healing in 11, 6% of cases [12].

The predominance of the absence of an appointment given by the physician, as a factor of non-compliance with the treatment in our study, could be explained by the lack of staff of the attending physicians on the one hand, and also the ignorance of the disease, treatments and follow-ups to be done by the patients on the other hand.

Lack of money was the third most common contributor to medication nonadherence in our study. A subsidy such as social security from the State could thus significantly improve the care of diabetics in Madagascar.

In our series, one in six patients had stopped their treatment following advice from a traditional practitioner. This remains an obstacle for the follow-up of treatment in our country. Indeed, the cost of care seemed less expensive for a traditional practitioner for the simplicity of their care. The latter had a great influence in Malagasy society. Rwegerera et al also confirmed this in their study that the use of traditional medicines was a cause of therapeutic nonadherence [29]. Ultimately, collaboration with traditional healers could reduce this non-compliance rate in order to improve the care of diabetics.

5. Conclusion

Non-adherence to therapy remains a major problem, especially in low-income countries like ours. According to the Morisky score, the prevalence of treatment nonadherence in our study population was 93.27%. It was mainly related to the

lack of control at the doctor, then the feeling of well-being, the lack of money, forgetfulness, and the advice of a traditional practitioner. Only getting an explanation of diabetes treatment from their doctor was significantly associated with adherence.

In view of its limitations, this study remains preliminary and superficial, so it requires further, more in-depth study. The ideal would be to conduct a multicenter study with more objective and more reproducible adherence measurement methods than the Morisky score to improve patient management.

Nevertheless, our results confirmed the important role that practitioners should play in ensuring better follow-up of diabetic patients. They should participate in improving the patient's therapeutic adherence by acting both at the level of the drug (compliance, adverse effects, etc.) and at the level of learning administration techniques and glycemic self-monitoring, or even psycho-social support for the patient.

Competing Interests

The authors declare that they have no competing interests.

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