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Analysis of adherence to pharmacotherapy by patients on hemodialysis treated at a university hospital

Análise da adesão à farmacoterapia por pacientes em terapia hemodialítica atendidos em um hospital universitário

DINIZ, Sávio Bruno Araújo[1]; NASCIMENTO, Felipe Cícero Pereira do[2]; BENVINDO, Mariana Martins[3]; MOREIRA, Francisca Sueli Monte[4]; SOUZA, Regina Meira Lima de de[5]; MATTA, Carolina Barbosa Brito da[6]

[1] 0000-0002-8085-8298; Hospital das Clínicas da Universidade Federal de Pernambuco (HC-UFPE). Recife, Pernambuco (PE), Brasil. saviodinizfarma@gmail.com
[2] 0000-0002-7423-4649; Universidade Federal de Pernambuco (UFPE). Recife, Pernambuco (PE), Brasil. felipe.cicero@ufpe.br
[3] 0000-0002-1454-707X; Hospital das Clínicas da Universidade Federal de Pernambuco (HC-UFPE). Recife, Pernambuco (PE), Brasil. marimartinsbenvindo@gmail.com
[4] 0000-0001-7069-750X; Universidade Federal de Pernambuco (UFPE). Recife, Pernambuco (PE), Brasil. francisca.sueli@ufpe.br
[5] 0000-0001-9735-7142; Hospital das Clínicas da Universidade Federal de Pernambuco (HC-UFPE). Recife, Pernambuco (PE), Brasil. reginameirahc@gmail.com
[6] 0000-0003-1917-4089; Hospital das Clínicas da Universidade Federal de Pernambuco (HC-UFPE). Recife, Pernambuco (PE), Brasil. carolinadamatta.hc@gmail.com

ABSTRACT

This study aimed to analyze adherence to pharmacotherapy by patients on hemodialysis treated at a university hospital. This is a descriptive, cross-sectional, prospective study with a quantitative approach; with data collection carried out between November 2022 and January 2023; which had sociodemographic and clinical data as variables and which used the Brief Medication Questionnaire (BMQ) to analyze the degree of adherence of the included patients. Those who did not obtain the minimum score for the Mini Mental State Examination cutoff points were excluded from the sample. Of the 43 patients included, there was a predominance of females (55.8%) aged over 50 years (53.5%), single marital status (41.9%), with family income of 1 to 3, 5 minimum wages (69.8%) and with more than 7 years of study (67.4%). The underlying diseases of undetermined etiology had the highest prevalence (18.6%). Among the participants, 53.5% had 1 to 3 comorbidities (3.7 ± 2.2) and had been on hemodialysis for less than 1 year (55.8%). Regarding the number of medications in use, there was a difference between the amount collected in the self-report (5.1 ± 2) and that obtained in the medical record (5.9 ± 2.4). Of these, 69.8% of the patients obtained a score compatible with low adherence according to the BMQ total score. In the "Regime" domain, 88.4% presented barriers. In the "Beliefs" domain, 27.9% scored and in the "Recall" domain, 93% obtained a score compatible with non-adherence. There was no statistically significant association between sociodemographic variables, however, there was a correlation between polypharmacy and non-adherence (p=0.027). The study enabled the identification of barriers to medication adherence, mainly in the domains "regime" and "recall".

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RESUMO

Este trabalho teve como objetivo analisar a adesão à farmacoterapia por pacientes em terapia hemodialítica atendidos em um hospital universitário. Trata-se de um estudo descritivo, transversal, prospectivo, com abordagem quantitativa; com coleta de dados realizada entre novembro de 2022 e janeiro de 2023; que teve como variáveis dados sociodemográficos e clínicos e que utilizou o *Brief Medication Questionnaire* (BMQ) para analisar o grau de adesão dos pacientes incluídos. Foram excluídos da amostra os que não obtiveram pontuação mínima para os pontos de corte do Mini Exame do Estado Mental. Dos 43 pacientes incluídos, constatou-se um predomínio do sexo feminino (55,8%) com idade maior que 50 anos (53,5%), estado civil solteiro (41,9%), com renda familiar de 1 a 3,5 salários mínimos (69,8%) e com mais de 7 anos de estudo (67,4%). As doenças de base de etiologia indeterminadas tiveram maior prevalência (18,6%). Entre os participantes, 53,5% possuíam de 1 a 3 comorbidades (3,7 ± 2,2) e estavam a menos de 1 ano em hemodiálise (55,8%). Referente ao número de medicamentos em uso, houve diferença entre a quantidade coletada no autorrelato (5,1 ± 2) da obtida no prontuário (5,9 ± 2,4). Destes, 69,8% dos pacientes obtiveram pontuação compatível com baixa adesão conforme score total do BMQ. No domínio "Regime", 88,4% apresentaram barreiras. No domínio "Crenças", 27,9% pontuaram e no domínio de "Recordação", 93% obtiveram um escore compatível com a não adesão. Não houve associação estatisticamente significativa entre as variáveis sociodemográficas, porém, verificou-se uma correlação entre polifarmácia e não adesão (p=0,027). O estudo possibilitou a identificação das barreiras à adesão medicamentosa, principalmente nos domínios "regime" e "recordação".

Palavras-Chave:
Adesão ao Tratamento Farmacológico, Hemodiálise, Cuidados Farmacêuticos.

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Introduction

Chronic Kidney Disease (CKD) corresponds to a general term for different changes that can affect kidney structure or function, having multiple causes and multiple prognostic factors, presenting in a clinically variable manner and generally having Renal Failure as the most serious outcome. (GO). Therefore, an individual is considered to have CKD who, regardless of the cause, presents a Glomerular Filtration Rate (GFR) < 60 mL/min/1.73m² for at least three consecutive months. In cases of patients with GFR ≤ 60 mL/min/1.73m², CKD is considered if associated with at least one marker of parenchymal renal damage (albuminuria, hematuria, electrolyte changes) or changes in the imaging exam (Brasil, 2014; Eknoyan *et al.*, 2013).

It is a disease with a prolonged, insidious course and, for most of its evolution, it is asymptomatic. CKD represents an important public health problem. In more advanced stages, it can lead to terminal chronic renal failure, making it necessary to use Renal Replacement Therapy (RRT), indicated for patients with a GFR below 10 mL/min/1.73m². Among the modalities, the RRTs used today are Peritoneal Dialysis (PD), Kidney Transplant (TxR) and, in greater numbers, Hemodialysis (HD) (Brasil, 2014; Pereira & Leite 2022).

HD, which consists of passing the patient's blood through a machine that removes excess nitrogen waste, water and mineral salts, promotes serum hydroelectrolytic homeostasis, continues to be the most adopted RRT. Data from the 2021 Brazilian Dialysis Census bring an estimated total of 148,363 dialysis patients. Of the prevalent patients, 94.2% were on HD, 5.8% on PD; 21% were on the waiting list for TxR (Elliott *et al.*, 2000; Saldanha *et al.*, 2022).

Even when the patient is already on HD or when the loss of renal function is inexorable, it is necessary to adopt measures to prevent the progression of CKD or to slow the rate of loss, using all clinical efforts to preserve GFR . Therapeutic measures must also be taken, as, throughout CKD, the emergence of conditions such as Bone Mineral Disorder (BMD), anemia and metabolic acidosis are expected, as well as cardiovascular diseases, resulting from the decline in GFR (Brasil, 2014; Eknoyan *et al.*, 2013).

For these reasons, a large proportion of patients who undergo HD use a considerable amount of medications from different therapeutic classes and with the most varied dosage schedules, thus generating many doubts, making adherence and, consequently, the effectiveness of the treatment even more difficult. Non-adherence to pharmacotherapy can also lead to failure to detect a true treatment effect in patients undergoing HD. Mirzaei-Alavijeh et al. (2023) highlight that dialysis patients use an average of 11 to 12 medications daily. In this sense, adherence to drug therapy has a positive effect on maintaining health,

quality of life and survival of hemodialysis patients (Murali et al., 2017; Sgnaolin & Figueiredo 2012).

The concept of membership is dynamic, complex and multidimensional; it can refer to drug treatment, diet or lifestyle change and is defined by the World Health Organization (WHO) as the degree to which an individual's behavior complies with the recommendations of health professionals. Referring to pharmacological treatment, non-adherence impairs the achievement of therapeutic results and, consequently, contributes to the progression of the disease, increasing morbidity, mortality and associated costs. Therapeutic ineffectiveness occurs in a significant portion of patients, therefore, it is necessary to adopt strategies to evaluate the pharmacotherapy used (Ghimire et al., 2015; Mirzaei-Alavijeh *et al.*, 2023; Oliboni & de Castro 2018).

Despite their low sensitivity and accuracy, questionnaires are the most used instruments to assess adherence to pharmacotherapy, as they have a relatively low cost and are feasible to apply to large populations. In Brazil, in 2012, the translation and reliability and performance assessment of the Brief Medication Questionaire (BMQ) was carried out. Brazilian studies with different audiences demonstrate the effectiveness of the BMQ in evaluating the adherence profile, including demonstrating greater sensitivity and specificity when compared to other questionnaires (Ben *et al.*, 2012; França *et al.*, 2020; Istilli, 2014).

Adherence to pharmacotherapy is one of the essential factors for the success of drug therapy. In the case of HD patients, it is essential in slowing morbidities that arise during CKD. Therefore, the study of factors associated with adherence is important so that successful intervention strategies can be implemented to improve adherence to pharmacotherapy among this population. Therefore, the objective of the present study was to analyze adherence to pharmacological treatment through a validated questionnaire and identify the main factors associated with non-adherence, as well as to understand the sociodemographic characteristics of patients undergoing hemodialysis in the hospital in question.

Methodology

Descriptive, cross-sectional, prospective study, with a quantitative approach, with data collection carried out between November 2022 and January 2023 in the hemodialysis sector of the *Hospital das Clínicas* of the Federal University of Pernambuco (HC-UFPE), whose sample was used for convenience.

Patients over 18 years of age of both genders were included; who had been on hemodialysis for more than 1 month; inserted into the HC-UFPE hemodialysis program, which serves around 70 patients; and who were available, with free and informed consent, to participate in the research and obtained a minimum score on the Mini Mental State Examination (MMSE). This test was used as an instrument for sample selection, as it analyzes

several domains (spatial and temporal orientation, immediate and recall memory, calculation, naming language, repetition and comprehension), evaluating the patient's cognitive capacity to respond to the other instruments. of the research. Depending on education, the following were considered as cut-off values: 18 points for illiterates, 21 points for 1-3 years of schooling, 24 for 4-7 years of schooling and 26 for more than 7 years of schooling (Caramelli & Nitrini 2000).

Patients who had a diagnosis or disabling factor that caused cognitive impairment were excluded, as well as those who were exclusively dependent on caregivers or companions, thus preventing the collection of the patient's own perceptions regarding their treatment and clinical condition.

Information was collected through medical records and an interview, using a questionnaire containing sociodemographic data (name and age, sex, race, marital status, education and income) and clinical data (underlying disease and comorbidities, years on hemodialysis and medications in use), an instrument to assess cognitive function (MMSE) and an instrument to measure patient adherence to pharmacological therapy, the Brief Medication Questionnaire (BMQ), which is a tool divided into three domains that identify barriers to adherence to the regimen , beliefs and memories regarding drug treatment from the patient's perspective. The analysis was carried out considering the total score of the instrument, in which no positive response indicates adherence to treatment, one positive response suggests probable adherence to treatment, two positive responses likely low adherence and three or more low adherence to treatment, and considering the score found in the three domains: Beliefs, Regime and Recall, with a score greater than or equal to one in any of these indicating a positive potential for non-adherence to treatment (Mantovani *et al.*, 2015).

After collection, pharmaceutical care was provided to the patient and a pamphlet made with information and care with medications was presented to the interviewee, reinforcing the importance of adhering to and knowing their treatment, setting up a moment for health education.

The collected data were tabulated using the Microsoft Office Excel® program. Categorical variables were presented as frequencies and percentages. Continuous variables were analyzed in the Statistical Package for the Social Science®, submitted to the Kolmogorov-Smirnov test (sample with N=43), and, as they did not follow a normal distribution ($p< 0.05$), the coefficient of Spearman correlation to verify the correlation of adherence (total BMQ score) with the variables age, sex, income, number of comorbidities, time on hemodialysis (years), polypharmacy (use of 4 or more medications) (Institute for Safe Practices in Use of Medicines [ISMP], 2019) and education (years). The research project was approved by the Research

Ethics Committee of the *Hospital das Clínicas* of the Federal University of Pernambuco, under CAAE number 63451222.7.0000.8807.

Results

From the 66 patients enrolled in the hemodialysis program (according to the November 2022 census), 3 were in transit during the collection period. Of the remaining 63 patients, 3 patients refused to participate in the research, 7 did not obtain a minimum score on the MMSE and 10 were excluded because they depended on a caregiver or had a diagnosis of cognitive impairment recorded in their medical records, with 43 participants ultimately being included in this research.

It was noted a predominance of females in the studied group (55.8%), with an average age of 51.8 years (± 14.3) with the majority over 50 years of age (53.5%), mixed race (48 .8%) single marital status (41.9%), with family income of 1 to 3.5 minimum wages (69.8%) and with more than 7 years of study (67.4%); as shown in Table 1.

Schedule 1.
Sociodemographic characterization of population in study

Sociodemographic variables	N	%
Gender		
Female	24	55,8
Male	19	44,2
Age		
≤50	20	46,5
> 50	23	53,5
Race		
Brown	21	48,8
Black	11	25,6
White	10	23,3
Oriental person	1	2,3
Status		
Single	18	41,9
Married	15	34,9
Stable union	7	16,3
Widower	2	4,7
Divorced	1	2,3
Family Income (Minimum Wages)		
<1	4	9,3
1 a 3,5	30	69,8
4 a 6	5	11,6
>6	1	9,3
Scholarity (Years in school)		
<1	2	4,7
1 a 3	3	7
4 a 7	9	20,9
>7	29	67,4

Source: Survey Data

Schedule 2 describes the clinical data of the patients included in the study. Basic diseases of undetermined etiology appeared with the highest prevalence (18.6%), followed by diabetes (16.3%). Among the participants, 53.5% had 1 to 3 comorbidities with an average of 3.7 (± 2.2) and had been on HD for less than 1 year (55.8%) with an average of 2.1 years on HD (± 3.8). Regarding the number of medications in use, there was a difference between the quantity collected in the self-report (5.1 ± 2), (ranging from 1 medication to a maximum of 8) and the number obtained in the medical record (5.9 ± 2.4) (ranging of 2 medications up to a maximum of 12), collected from the patient's most recent prescription.

Schedule 2.

Clinical Characterization of population in study

Clinical variables	N	%
Underline Disease		
Undertemided Etiology	8	18,6
Diabetes	7	16,3
Hypertension	5	11,6
Glomerulopathies	5	11,6
Neoplasia / Cancer	5	11,6
Polycystic Kidney Disease	4	9,3
Lupus	3	7
Nephrolithiasis	2	4,7
Sickle cell Anemia falciforme	1	2,3
Neurogenica bladder	1	2,3
Renal Tuberculosis	1	2,3
Scleroderma Renal Crisis	1	2,3
Comorbities		
1 a 3	23	53,5
4 a 6	13	30,2
>6	7	16,3
Hemodialysis (years)		
< 1	24	55,8
1 a 5	14	32,6
6 a 10	3	7
>10	2	4,7

Source: Survey Data

When analyzing patient adherence according to the total BMQ score, 69.8% of patients obtained a score compatible with low adherence. In the “Regimen” domain, which deals with difficulties related to the correct identification of medications in use as well as dosage errors, 88.4% of respondents presented barriers to adherence (score≥1). In the “Beliefs” domain, which points to the patient’s confidence in the treatment and brings up adverse reactions, 27.9% of patients demonstrated barriers (score≥1) and in the “Recall” domain, which refers to

the use of multiple doses daily and as well as difficulties remembering to take medications, 93% had a score equivalent to non-adherence (score≥1) (Table 3) (KASPER *et al.*, 2017; Mantovani *et al.*, 2015).

Schedule 3.

Distribution of participants according to medication adherence variables

SCORE BMQ	N	%
Escore Total		
Accession (0)	0	0,0
Probable accession (1)	8	18,6
Low probable accession (2)	5	11,6
Low accession (3 or more)	30	69,8
Score by domain		
Regime		
0	5	11,6
≥1	38	88,4
Beliefs		
0	31	72,1
≥1	12	27,9
Memory		
0	3	7,0
≥1	40	93,0

Source: Survey Data

Regarding positive responses (which indicate lower adherence), 67.4% failed to list the medications prescribed in the regimen domain; 16.3% named the medications that bother them in the beliefs domain and 93% receive a regimen of multiple doses of medication (2 or more times/day) in the memory domain; as shown in Schedule 4.

Schedule 4.

Positive responses per questions in each BMQ domain

Domains	N	%
DR - Regime		
DR1. Did R fail to (spontaneously) list the prescribed medications in the inicial report?	29	67,4
DR2. Did R stop therapy due to delay in dispensing medication or another reason?	20	46,5
DR3. Did R report any missed days or doses?	15	34,9

DR4. Did R reduce or omit doses of any medication?	3	7
DR5. Did R take any extra doses or more medication than prescribed?	1	2,3
DR6. Did R respond that "didn't know " to any question?	1	2,3
DR7. Did R refuse to answer any question?	0	0
DC –Beliefs		
DC1. Did O R report "doesn't work well " or "doesn't know " in answer 1g?	6	14
DC2. Did R name the medications that bother him?	7	16,3
DRE –Memory		
DRE1. Does R receive a multiple dose regimen of medication (2 or more times/day)?	40	93
DRE2. Does R report "a lot of difficulty " or "some difficulty " in answering 3c?	15	34,9

Source: Survey Data - Adapted from Ben et al. (2012)

Analysis of the correlation between adherence (total BMQ score) with age, sex, income, number of comorbidities, time on hemodialysis (years), polypharmacy (use of 4 or more medications) (ISMP, 2019) and education (years) (Schedule 5), found a positive correlation between polypharmacy and non-adherence (p=0.027).

Schedule 5.

Correlation test with collected variables

Variable	Spearman Coefficient	By value
Age	-0,163	0,297
Gender	0,065	0,677
Income	-0,026	0,869
Comorbities quantity	0,002	0,992
Hemodialysis (years)	0,116	0,457
Polypharmacy	0,338	0,027
Scholarity (Years in school)	-0,03	0,849

Note: By Value When p< 0,05

Discussion

The present study showed that non-adherence to medication treatment is frequent in the included patients, being a common finding among patients with CKD who undergo HD (Bampi et al., 2015; Pereira & Leite 2022; Sgnaolin & Figueiredo 2012). According to the instrument used, 69.8% of patients obtained a score compatible with low adherence. The main barrier found was in the "Recall" domain, as 93% of patients receive a multiple dose regimen of medication (2 or more times/day). The second biggest barrier found was in the "Regimen" domain, where 67.4% failed to correctly list the prescribed medications. In this area, attention is also drawn to the fact that 46.5% of respondents interrupted therapy due to delays in dispensing medication or another reason.

The use of multiple doses of different medications during the day is common in patients undergoing HD because they generally have chronic comorbidities, which require the use of multiple medications and, therefore, place them at high risk of polypharmacy. This fact requires greater attention, memory and organization from the patient regarding the administration times of the medications they use (Bampi et al., 2015; Paneerselvam et al., 2022).

Bampi *et al.* (2015) evaluated medication adherence in patients with chronic renal failure on hemodialysis and found 65% with low adherence and 35% with probable low adherence, also using the BMQ. In a study carried out in Iran, Mirzaei-Alavijeh et al. (2023), using the COM-B model to identify the determinants of medication adherence among patients with end-stage renal failure, obtained an indication of 59.7% of these with the maximum score for adherence among the 260 HD patients included in the study. However, the authors highlight other studies that report treatment adherence rates of less than 50%.

On the other hand, a study (Albarelo *et al.*, 2020) that evaluated adherence to the treatment of systemic arterial hypertension of patients participating in the hyperdia program of a family health strategy found with the BMQ that 22.9% of respondents actually have adherence to medication treatment for hypertension and 47.8% are likely to adhere; while 28.2% have probable low adherence and 1.2% have low adherence. This discrepancy indicates that adherence to treatment is related to particular characteristics, varying by population and pathology under study, for example.

It was observed in the group that underlying diseases of undetermined etiology appeared with greater prevalence (18.6%), followed by diabetes (16.3%). Regarding the underlying diagnosis of CKD, other studies showed that 43.1% had the disease with an undetermined cause, followed by diabetic nephropathy (de Oliveira et al., 2022). According to the 2021 Brazilian Dialysis Census, the diagnosis rate of underlying diseases remained stable, with hypertension accounting for 32% and diabetes for 30%, however, due to the difficulty in establishing the primary diagnosis of CKD, it appears that diabetes has not surpassed

hypertension as the main primary disease in Brazil in previous research. In contrast, diabetes was the leading primary diagnosis in the United States dialysis population in 2017 (45%), while hypertension accounted for 30% (Saldanha *et al.*, 2022).

As in our study, Sgnaolin & Figueiredo (2012) also found differences in the number of self-reported and prescribed medications and only a minority of patients correctly reported the name and dose of all prescribed medications. The patient's knowledge about the pharmacotherapy in use is also a factor that directly influences the level of adherence (Sgnaolin & Figueiredo 2012). Due to the complexity of CKD, the HD patient must be empowered to be an active agent in decision-making. To this end, providing elements that support decision-making regarding available care is a responsibility of health services. The lack of communication and indifference of health professionals are representative of lack of empowerment (Almeida *et al.* 2019).

Interruption in therapy, whether due to delay in dispensing medication or another reason, was another important finding. Thus, the way in which medications are obtained may be associated with lower adherence rates, as the majority of our sample acquires medications only through the SUS or buys and receives them in the public network, through the Specialized Component of Pharmaceutical Assistance (CEAF), which enables obtaining expensive medications for the treatment of patients on dialysis CKD, constituting the SUS strategy that aims to guarantee the completeness of medication treatment (da Hora Brito & de Araújo 2022).

Da Hora Brito & de Araújo (2022) point out in their study that the difficulties encountered in accessing medicines were related to the lack of medicine, information, as well as bureaucracy and delay. Factors such as the absence or outdated clinical examinations, which result in the majority of medication requests being rejected, lack of information on documents necessary for registration or the inclusion of a new drug end up delaying the dispensing of the medication (Pimentel *et al.* , 2022).

When evaluating medication adherence in patients with systemic lupus erythematosus in the same hospital where this study was developed, Assis (2019) found that the main reasons for reported difficulties in taking medications were the impossibility of purchasing and not being able to acquire the medications through the SUS.

There was no statistically significant association between the sociodemographic variables collected in this study (age, sex, income, number of comorbidities, time on hemodialysis and education and patient adherence ($p>0.05$), suggesting that these variables were not factors that directly influenced the adherence of patients in the study group. França et al. (2019), when using the BMQ to evaluate the adherence of patients new to antiretroviral therapy, found no association between its score and the variables gender, race, degree of education, marital status and age. Albarello *et al.* (2020), when evaluating adherence to

systemic arterial hypertension treatment, did not find statistical significance between adherence to drug treatment (using the BMQ) and age, sex, education and family income. There are others studies, such as Jacques *et al.* (2015), which also found no statistical association between some sociodemographic variables and the adherence profile of the studied population.

Data from the literature indicate that the lack of association can be explained by the fact that each disease or treatment has its specific adherence barriers and the factors that relate to lack of adherence are not only linked to the medication, but also to individual characteristics, being a dynamic process, influenced simultaneously by economic and social factors, health system and team, characteristics of the disease, type of therapy and factors related to the patient (França et al., 2020; Pereira & Leite 2022).

In this study, there was a positive correlation between polypharmacy and non-adherence (p=0.027). The negative effect of polypharmacy on adherence is already known, as a complex treatment requires greater dedication from the patient, correct follow-up of instructions and perception of the importance of the treatment for maintaining their life. Therefore, the large number of medications can lead to non-compliance with treatment or forgetting to take some medications, resulting in low adherence (Bampi *et al.*, 2015; Gewehr *et al.*, 2018).

It is highlighted in the literature that the presence of the pharmacist in the care of patients with CKD undergoing HD provides an improvement in medication adherence, reduces Medication-Related Problems (DRPs) and optimizes therapeutic results, with the presence of this professional in the multidisciplinary teams that monitor kidney patients (Bampi *et al.*, 2015; Paneerselvam *et al.*, 2022).

The BMQ proved to be important in monitoring the adherence of this group of patients, however it is necessary to associate it with other measures for it to be truly effective, as well as the development of research to evaluate the portion of patients not included in this study, as family members and Caregivers can facilitate adherence to treatment by assisting with pharmacotherapy and influencing the mechanisms that favor self-care (Albarelo *et al.*, 2020; Almeida *et al.* 2019).

The main limitations of this study are inherent to an analysis limited to a single University Hospital, the sample size and bias in data collection from medical records, as they were physical records. Other limitations of the research refer to those inherent to the use of interviews, linked to the investigation device, the interviewer-interviewee relationship and the research context (Moura & Rocha 2017). To this end, the information collected in the medical records at the time of the interview was confirmed and the recommendations of the original

article were followed during data collection. There are still few studies that provide information on the adherence profile of hemodialysis patients in Brazil, therefore the data analyzed support new research on this topic.

Final Considerations

The study demonstrated that a significant portion of the participants in this research had difficulty adhering to the proposed treatment, affecting the survival and quality of life of HD patients, therefore being a cause for concern.

In this sense, the analysis carried out made it possible to identify the barriers interfering with medication adherence by the study population as well as a sociodemographic and adherence profile, allowing a better understanding of the determining factors for effective adherence. Such data impacts interprofessional practice, as in addition to being relevant due to the public health system's high investment in medicines, it provides information for better team performance in the patient's drug therapy.

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