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**ADHERENCE TO DRUG THERAPY IN PATIENTS WITH CORONARY
ARTERY DISEASE**

**ADESÃO À TERAPÊUTICA MEDICAMENTOSA DE PACIENTES
PORTADORES DE DOENÇA ARTERIAL CORONÁRIA**

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ABSTRACT - In this study the adherence to drug therapy of patients with coronary artery disease was analyzed. A total of 48 patients participated in this study, who provided information on their socioeconomic profile and adherence to drug therapy through a questionnaire. The analysis was carried out using the STATA version 10.0 statistical software. Platelet aggregation inhibitors and beta-blockers were the drugs most commonly used in treatment. According to the convergence between the use of medicine and the medical prescription, 19% adhered to the treatment and 81% failed to adhere. Among the factors that interfered with adherence to treatment are age (54.17%),

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followed by forgetfulness (52.08%) and cultural aspects (43.75%). The prevalence of non-adherence and the use of large quantities of medicine are still challenges for the National Health System. These findings reveal the need to implement policies regarding ease of access and awareness of appropriate use of medicines, in order to reduce the percentage of non-adherence to drug treatment.

Keywords: Heart Disease; Patient Non-Adherence; Treatment Failure.

RESUMO - Neste estudo foi analisada a adesão à terapêutica medicamentosa de pacientes portadores de Doenças Arteriais Coronarianas. Participaram deste estudo 48 pacientes, os quais forneceram informações do perfil sócio econômico e acerca da adesão à terapia medicamentosa através de questionário. Na análise empregou-se o programa estatístico STATA versão 10.0. Os inibidores da agregação plaquetária e os agentes betabloqueadores foram os medicamentos mais utilizados no tratamento. De acordo com a convergência da tomada do medicamento com a prescrição médica, observou-se 19% de adesão e 81% de não adesão ao tratamento. Dentre os fatores que interferiram na adesão ao tratamento estão a idade (54,17%), seguido do esquecimento (52,08%,) e dos aspectos culturais (43,75%). A prevalência da não adesão e a utilização de grande quantidade de medicamentos ainda continuam como desafio para o Sistema Único de Saúde. Estes achados revelam a necessidade da implementação de políticas que envolvam a facilidade ao acesso, e a sensibilização da utilização adequada dos medicamentos de forma a reduzir o percentual da não adesão ao tratamento medicamentoso.

Palavras-chave: Doenças Cardíacas; Adesão à Medicação e Falha de tratamento.

INTRODUCTION

According to the World Health Organization (WHO), approximately 17.9 million people died in 2017 from cardiovascular diseases, 31% of overall deaths, of which 7.5 millions of these were due to coronary heart disease. Estimates for 2030 predict that 23.6 million people will die from cardiovascular diseases, with about 80% of these occurring in low- and middle-income countries (WHO, 2017). In Brazil,



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cardiovascular diseases account for 23,14% of prevalent deaths having known causes, surpassing vascular brain diseases (16.17%), infectious respiratory diseases (11.07%) and Alzheimer and other dementia (9.67%) (BRASIL, 2017). Approximately one-third of deaths from cardiovascular disease occur early in adults aged 35-64 years old. The treatment of coronary artery disease (CAD) presents a challenge to clinical practice, because it involves changes in behavior and lifestyle, and principally, the use of medications over long periods, or even for life. Despite the evidence that antihypertensive treatment is effective in reducing cardiovascular morbidity, mortality and rates of blood pressure, the disease control is low because of the low level of adherence to treatment (LANDIM *et al.*, 2011).

The use of medicine is influenced by the demographic structure, socioeconomic, behavioral, and cultural factors, as well as characteristics of the pharmaceutical market and governmental health care policies. Few studies regarding the interference of the factors in the adherence to treatment for a variety of diseases refer to adherence to drug therapy. The available data on adherence in Brazil and in the world are scarce, and those that exist were obtained from different population types using a variety of criteria (BASTOS-BARBOSA *et al.*, 2012). In this context, adherence to therapy is discussed as an important component of resolving treatment.

Adherence to treatment can be understood, according to the definition proposed by the World Health Organization, as "the degree to which the behavior of a person, represented by the intake of medication and compliance with dietary and lifestyle changes, corresponds and agrees with the recommendations of a doctor or other health professional." Failure to adhere to drug treatment is the principal cause of treatment failure, irrational use of medications, and aggravations in the pathological process, resulting in higher public health costs due to an increase in poisoning cases and hospital admissions. It is estimated that around 50% of patients living with chronic diseases do not properly follow their treatment. Studies that identify the frequency of medicine use and the motives for non-adherence to treatment could contribute to the detection of difficulties and/or problems with the health care services provided to the general population. They would also allow for the identification of the groups most likely to fail to adhere to treatment, making possible the adoption of actions directed towards these groups to stimulate habits that will improve quality of life.

The Adherence Project of the WHO defines adherence to treatment as the degree to which a person's behavior, represented by ingesting medicine, following a diet, and changing lifestyle habits, corresponds and agrees with the recommendations of a doctor



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or other healthcare professional (GUSMÃO and JUNIOR, 2006). Meanwhile, adherence to medication is defined by Carvalho and collaborators (CARVALHO *et al.*, 2012) as inherent behaviors towards health that range from simply following a drug prescription to involve aspects related to the healthcare system, socioeconomic factors, and aspects related to treatment, to the patient, and to the disease itself. This last concept was the one used for this study, as the objective was to evaluate adherence to therapeutic medications by CAD patients in a city in the Recôncavo da Bahia region.

MATERIALS AND METHODS

The present study was carried out in Santo Antônio de Jesus located in the state of Bahia. The methodology used consisted of a descriptive exploratory study utilizing a quantitative approach, that sought to analyze the adherence to therapeutic medicine of CAD patients. This study is a cohort of a larger project entitled Correlation of Genetic Polymorphism of Lipoprotein Lipase and Neuropeptide Y in Dyslipidemia and Coronary Artery Disease. The subjects of the study include patients older than 18 with CAD confirmed by laboratory and clinical diagnosis with authorized medical opinion, who are using medications associated with cardiac comorbidity. Data were collected from standardized interviews through the application of a specific questionnaire.

Non-adherence to medical treatment was considered to be a dependent variable. In order to assess this variable, the Morisky questionnaire (MORISKY *et al.*, 1986) was used and data collection was supplemented using Sarquis (SARQUIS *et al.*, 1998) as a reference. Also, during the interviews, each patient was asked to show their last prescription with the medications prescribed by the doctor. The manner in which each drug was taken was questioned so that the patient could indicate, in the case of non-adherence, the specific medication(s) that were not taken according to the medical prescription. In this way, the Medication Taken and Prescribed (MTP) variable was created, establishing the following criteria: Cases where the patient followed the treatment exactly as prescribed were considered as adherence to treatment. When the patient did not follow the treatment exactly as prescribed, it was considered to be non-adherence to treatment. The results were analyzed using an ordinal measure, with high adherence for those responding negatively to the first four questions, medium adherence for those who responded affirmatively to one or two questions, and low adherence for those responding affirmatively to three or four questions.



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The following variables were also evaluated: socio-demographic characteristics according to the Brazilian Institute of Geography and Statistics, clinical characteristics and medication characteristics. Among the variables related to factors that interfere with patient adherence, this study considered whether structural factors, such as age, education, cultural aspects (beliefs, lifestyle habits), lack of knowledge about the disease, forgetfulness, family support or others interfered with adherence to pharmacological therapy. Regarding factors related to medical treatment, it was asked whether dosage, quantity of medication, collateral effects, prolonged treatment, cost, among others, interfered with adherence to pharmacological therapy.

Statistical analysis was performed using the Stata statistical program, version 10.0 (Stata Corp., College Station, United States). The study was approved by the Research Ethics Committee of the State University of Santa Cruz-Bahia, under protocol 324/09, with the authorization of the Institute of Cardiology of Recôncavo (INCAR) and the authorization of the participants through the signing of the free and informed consent form.

RESULTS

Considering the socio-demographic aspects (Table 1), the study sample of 48 individuals was 72.92% male. Ages ranged from 47 to 82, however, the majority of participants (70.83%) were older than 60, with an average age of 64.2 years (SD = 8.35). With regard to schooling, the majority had not completed high school (60.42%), while 8.33% had completed a university degree, 12.50% were illiterate, and the smallest portion (2.08%) had completed high school but not any higher education. Looking at average income, 41.66% of the individuals received between one and three times the minimum wage, while 22.92% received less than one minimum wage.



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Table 1. Socio-demographic characteristics of individuals with CAD attended in the municipality of Santo Antônio de Jesus (BA), Brazil

Characteristics	Absolute frequency (N=48)	Relative Frequency (%)
Gender		
Male	35	72.92
Female	13	27.08
Age range		
< 60	14	29.17
≥ 60	34	70.83
Education level		
Illiterate	06	12.5
Incomplete elementary school	29	60.42
Complete elementary school	01	2.08
Incomplete high school	04	8.33
Incomplete university graduation	01	2.08
Complete university graduation	04	8.33
Post Graduation	03	6.25
Income		
Less than a minimum wage	11	22.92
1 to 3 minimum wages	20	41.66
3 to 5 minimum wages	03	6.25
5 to 7 minimum wages	03	6.25
7 to 10 minimum wages	05	9.70
10 or more minimum wages	06	12.50

Source: Primary data.

With regard to clinical characteristics, medications and factors that interfere with adherence to treatment, among associated diseases, it was observed that 17 (35.42%) of the individuals with CAD also suffered from diabetes mellitus, 43 (89.58%) suffered from hypertension, 22 (45.83%) had high triglycerides, and 38 (79.17%) had high cholesterol. With regard to the consumption of medication, 100% of those interviewed used drugs to treat CAD. Platelet aggregation inhibitors (acetylsalicylic acid) and beta blockers (atenolol) had the highest rate of use (16.67% each), followed by selective beta



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blocking agents (Metoprolol) and ACE inhibitors (Captopril) with 14.58% each. Peptic ulcer drugs (omeprazol), alpha and beta blockers (carvedilol), and single angiotensin II antagonists (losartan) were each used by 6.25% of the patients. Lipid modifying agents (atorvastatin) and sulfonamides / urea derivatives (glibenclamide) had a frequency of use of 4.17%, each. The least used classes of drugs were preparations of bile acids (ursodeoxycholic acid), glucose-lowering drugs (acarbose), antivirals, corticosteroids, and dopamine agonists (2.08%, each). With regard to the total number of medications prescribed, the minimum quantity was two and the maximum was eleven, with an average of 6.2 and a median of 6.5 medications.

When analyzing adherence to treatment by the criteria suggested in this study, based on Morisky's proposal (SARQUIS et al., 1998) considering three treatment adherence subgroups (total/partial/none), it was observed that the majority (79.17%) was partially adherent (Table 2). Using the classification of treatment adherence based on convergence with the medical prescription, it was found that 19% of the interviewees were adherent and 81% were non-adherent.



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Table 2. Distribution of patients according to adherence to drug therapy, personal and socioeconomic characteristics. Santo Antonio de Jesus (BA), Brazil

Variables	Patient Adhesion		
	Total (%/N)	Partial (%/N)	None (%/N)
Gender	18.75%(9)	79.17%(38)	2.08%(1)
Male	17.14 %(6)	80.00 % (28)	2.86% (1)
Female	23.08 %(3)	76.92 % (10)	0.0 % (0)
Education level			
Illiterate (N=6)	33.33 % (2)	66.67%(4)	0.0%
Incomplete elementary school (N=29)	17.24% (5)	79.31(23)	3.45% (1)
Complete elementary school (N=1)	100% (1)	0.0%	0.0%
Incomplete high school (N=4)	0.0%	100%(4)	0.0%
Incomplete university graduation (N=1)	0.0%	100%(1)	0.0%
Complete university graduation (N=4)	0.0%	100%(4)	0.0%
Post Graduation (N=3)	33.33% (1)	66.67(2)	0.0%
Race			
White (N=18)	33.33%(6)	66.67%(12)	0.0%
Black (N=12)	8.33% (1)	83.33%(10)	8.33%(1)
Pale brown (N=17)	11.76%(2)	88.24%(15)	0.0%
Other (N=01)	0.0%	100%(1)	0.0%
Age range			
< 60	7.14%(1)	92.86%(13)	0.0%
> 60	23.53%(8)	73.53%(25)	2.94%(1)

Source: Primary data.

Relating adherence to medication with the independent variables, it can be seen that the majority for both sexes fell within the partial adherence category. Women had



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the highest total adherence rate (23.08%), compared to 17.14% for men. Comparing adherence with level of education, illiterate individuals had the same rates of adherence in the three categories (total, partial, none) as those with postgraduate / master's / doctoral degrees, being 33.33%, 66.67%, and 0.00% for both. With regard to race, whites had the highest adherence percentage, with 66.67% in the partial adherence category, and 33.3% total adherence, while mixed-race individuals had 88.24% partial adherence. Regarding age groups, it was found that both groups fell mostly into the partial adherence category, with 92.86% and 73.53%, respectively.

Regarding the patient-related factors (Table 3), all patients reported that some of these factors could interfere in their adherence to treatment, with lack of knowledge about the disease indicated by 27 (56.25%) of the interviewees, who reported this as a preponderant factor that could make adherence to therapy difficult. The other factors most frequently mentioned were age (54.17%), forgetfulness (52.08%), and cultural aspects (43.75%). Among those not considered to interfere with medical treatment, the most often cited were education (64.58%), culture (56.25%), and family support (66.67%).



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Table 3: Study participants according to factors related to drug treatment and interfering with treatment adherence, Santo Antônio de Jesus (BA), Brazil

Study Variables	Yes%(N)	No%(N)
Patient Related		
Age	54.17% (26)	45.83% (22)
Educational	35.42% (17)	64.58% (31)
Cultural aspects	43.75% (21)	56.25% (27)
Ignorance about the disease	56.25% (27)	43.75% (21)
Forgetfulness	52.08% (25)	47.92% (23)
Family support	33.33% (16)	66.67% (32)
Related to drug treatment		
Dose	35.42% (17)	64.58% (31)
Number of Medicines	47.92% (23)	52.08% (25)
Side effects	35.42% (17)	64.58% (31)
Prolonged treatment	56.25% (27)	43.75% (21)
Expense	75.00% (36)	25.00% (12)
Medicine change	14.58% (07)	85.42% (41)
Drug Effectiveness	35.42% (17)	64.58% (31)
Medication Schedules	35.42% (17)	64.58% (31)
Symptom improvement	14.58% (07)	85.42% (41)

Source: Primary data.

As for the medication-related factors that can interfere with medical treatment, the most cited were cost (75%), prolonged treatment (56.25%), and quantity of medicines (47.92%). When questioned about which factors did not interfere with adherence to medical treatment, the most important were dosage (64.58%), side effects (64.58%), change of medication (85.42%), drug effectiveness (64.58%), medication schedule (64.58%), and improvement of symptoms (85.42%). Three other factors were evaluated (family care, form of acquisition of medication, and cost of medication), with social and family involvement being referred to by 66.67% of patients as important, principally in remembering the hours for taking medicines. Regarding availability of medications, 31.25% of those interviewed were able to obtain all of their prescribed medications through the public health service, with the other 68.75% obtaining their medicines on their own.



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DISCUSSION

The socio-demographic characteristics found were similar to those related by Jousilahti in a study with 14,786 people, which demonstrated an incidence rate for CAD of 786/100,000 for males and 256/100,000 for females, indicating a risk of CAD in men approximately three times higher than in women (JOUSILAHTI *et al.*, 1999). Steffens affirmed in his study that the risk of cardiovascular disease doubles after age 55, which agrees with the data found in this study, where the average age was 64.2 years (STEFFENS, 2010). A cross-sectional cohort study conducted in the city of Salvador-Bahia by Gama found that 52.00% of the group of people affected by CAD had a low level of education, with 34.00% unschooled and 53.00% with education up to elementary school (GAMA *et al.*, 2011). Another study carried out in Great Britain analyzed the different social classes and their relation to deaths from CVD and the authors conclude that the mortality rate is higher among the lower classes (MARANGVAN *et al.*, 1998). These data indicate that a low education level may reflect a lower socioeconomic level, hindering the process of understanding the disease (CORRÊA *et al.*, 2010).

Regarding clinical parameters, there was a predominant association between CAD and arterial hypertension (89.58%) and diabetes *mellitus* (35.42%). Equivalent values were found by Gama with 94.0% of individuals having arterial hypertension associated with CAD and 35.0% of individuals with CAD having glucose indexes outside the normal range (GAMA *et al.*, 2011).

In Brazil, the use of a great number of medications by individuals over the age of 60 can be observed. In this sample, the average number of medications used per individual was 6.2, a value higher than that described by Silva (SILVA *et al.*, 2012) and by Flores and Mengue, with 3.8 and 3.2, respectively. The most commonly-used drugs for the treatment of CAD were platelet aggregation inhibitors and beta-blockers, each used by 16.6% of the patients, a value similar to the data described by Oliveira (OLIVEIRA *et al.*, 2009). With regard to selective beta-blocking agents and ACE inhibitors, this study found a lower rate of use (14.58%) when compared to the study by Reinhardt (REINHARDT *et al.*, 2012). The Brazilian Health Ministry (BRASIL, 2012), describes states that representatives of ACE inhibitors and angiotensin receptor antagonists have been shown to be effective in preventing cardiovascular events in patients with diabetes or who have had previous cardiovascular events, regardless of



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blood pressure, making them the drugs of choice in these situations. Furthermore, studies have shown that hypertension is a reversible risk factor and that reducing blood pressure through medication reduces the risk of cardiovascular events (SCOTTI *et al.*, 2013). Lipid-modifying agents and the hypoglycemic agents sulfonamide / urea derivatives were each used by 4.17% of patients, a low percentage low when compared with the percentage of individuals who reported having high cholesterol and triglycerides, 45.83% and 79.17%, respectively. In a study conducted by Girardi statins were prescribed for 87.1% of patients, with simvastatin the most frequently prescribed drug (71.2%). The use of these drugs may be justified by the presence of possible comorbidities associated with the elderly population (GIRARDI *et al.*, 2011).

The analysis of adherence to medication in this study differs from that found by Medeiros, where 25.8% of the interviewees were totally adherent, 50.8% were partially adherent, and 22.5% were non-adherent. Still, in this study 22.92% of patients interrupted their medication use at least one time. Of these, 72.72% stopped taking the drug for less than three days (MEDEIROS and VIANNA, 2006). In a meta-analysis of 376,162 patients, Sayed relate that after 24 months, non-adherence to treatment was 43% (SAYED *et al.*, 2012), while Hermano found 50.8% classified as potentially non-adherent and 37.7% as non-adherent to treatment (HERMANO *et al.*, 2021). Coleta affirms that non-adherence could be related to behavioral factors (COLETA *et al.*, 2010). When classifying adherence to drug treatment according to convergence with the medical prescription, results were similar to those found by Medeiros and Vianna (2006).

The group studied in this research presented homogeneous characteristics when evaluating adherence against socio-demographic variables. Contrary to these findings, Gama observed that the majority of individuals who did not fully comply with the medical prescription were illiterate. When relating age with adherence, those over 60 years of age had a 92.86% rate of partial or high adhesion, which fell to 73.53% for those younger than 60. The structural factor that interfered with adherence to treatment the most was age (54.17%), followed by forgetfulness (52.08%) and cultural aspects (43.75%) (GAMA *et al.*, 2010). In a study conducted by Bastos-Barbosa 42% of the elderly had no knowledge of the chronic nature of hypertension. Patients with controlled hypertension were more knowledgeable about the duration of the disease than those whose hypertension was uncontrolled (BASTOS-BARBOSA *et al.*, 2012). The study by Gama pointed to forgetfulness (26.4%) and personal limitation with regard to reading the prescription (14.2%) as factors for incorrectly taking prescribed medications,



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demonstrating dependence on others for correct use, as well as being associated with the age structural factor (GAMA *et al.*, 2011). Carvalho *et al.* (2012) study also points to forgetfulness as one of the principal causes of non-adherence.

In this study, factors that interfere with adherence, such as cost (75%), prolonged treatment (56.25%), and quantity of medicines (47.92%), agree with the study by Sayed, where among the factors making adherence difficult, once again, the cost and quantity of medicines taken stand out (SAYED *et al.*, 2012). Sarquis *et al.* reported that the cost of antihypertensive drugs appeared to be a frequent impediment to effective therapy. They also add that patients with problems affording medication in general are of a non-privileged socioeconomic level and appear to have greater morbidity and a greater frequency of strokes and heart problems than those without financial problems (SARQUIS *et al.*, 1998). Among the factors facilitating adherence were low doses (64.58%), absence of side-effects (63.58%), changes in medication (85.42%), drug efficacy (64.58%), schedule of medications (64.58%) and improvement of symptoms (85.42%). A low level of adherence to medication also has been associated with decreased control of arterial hypertension and diabetes (COLETA, 2010), low clinical outcomes, increase in the cost of healthcare, and consequences for the productive workforce and public health (BOSWORTH *et al.*, 2011). In order to improve and support adherence to medical treatment for individuals with CAD, it is necessary to prescribe medications with fewer side-effects, lower cost, administered in the fewest possible number of doses, and with a medication schedule that fits the individual's daily routine. The elaboration of collective and individual strategies must be based on the best available scientific evidence, adapted to the reality of the services. In this sense, health professionals need to pay attention to social and economic issues, in order to implement and evaluate care that, in fact, contributes to self-care and better adherence to the therapeutic regimen. In addition, family members are important to remember the timing of medication, as reported by 66.67% of individuals in study by Santa-Helena *et al.* (2010). Saraiva *et al.* (2007) affirm that the family is the first recourse patients look to when dealing with problems. This family support can consist of simple meal preparation, leisure, or help with the medication routine and health evaluation consultations. However, his study concluded that, many times, the family caregiver is often pressured to adopt significant lifestyle changes, which usually demands a great deal of energy, tolerance and goodwill. Therefore, public health policies should be thought of as a way to favor the access and permanence of the CAD patient in



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treatment, as well as to provide support so that the family can participate effectively in care giving.

Regarding the availability of medicines, 31.25% of the interviewees get all their prescribed drugs from the public health service clinics, and the other 68.75% get their medicines on their own. Halfoun *et al.* (2012) stated that the availability of medications in the patient supply services was seen in their study as an antecedent to antihypertensive treatment adherence. Bueno *et al.* (2012) also show that generic drugs and drugs from the Popular Pharmacy of Brazil are easily accessed by the population, contributing to the continuity of pharmacotherapy when unavailable through the Unified Health System and/or when patients lack sufficient income to purchase medicine on a regular basis. Access to medicines should be considered at the time of prescription, especially by those employed in the treatment of chronic diseases. Therefore, it is understood that the public production of medicines and their free supply is an important strategy of assistance to the populace. A higher level of adherence reduces coronary artery disease, mortality, hospital readmissions, and costs (BITTON *et al.*, 2013). Thus, programs that reduce costs are important, since they can help patients acquire medicines and increase the rates of adherence.

CONCLUSIONS

Regarding the question of adherence to drug treatment, it can be seen that there are many issues involved in its success or failure, involving a multiplicity of complex factors, which require all involved to use a combination of strategies. These results show that the prevalence of non-adherence, as well as the use of large quantities of medicines, remains a challenge for the Unified Health System. They also reveal the need to implement policies to improve ease-of-access and raise awareness of the proper use of medications in order to reduce the rate of non-adherence. The adoption of educational strategies to help the patient adhere to treatment becomes essential, requiring patience and dedication on the part of the professionals involved, as well as family members. Health education is important for the protection and promotion of health, enabling individuals to be healthier, reducing the risks of cardiovascular diseases and reducing the number of illnesses and deaths. In addition, preventive measures and healthy lifestyle habits improve the quality of life of the population and reduce direct and indirect costs.



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Adherence to drug therapy does not depend only on the creation of policies and/or programs for the prevention of cardiovascular diseases, which may not in themselves guarantee the problem's resolution. The adherence by the user to the proposed therapeutic regimen is necessary. It is important to consider that many of the participants of this study suffer from CAD and have already developed serious complications associated with it and have still not adhered adequately to the drug therapy. Therefore, the data presented here deserve the attention of all health professionals, because despite the fact that these individuals are monitored for these diseases by a referral service, the percentage of non-adherence to the proposed therapy was still high.

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