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RESEARCH ARTICLE

ADHERENCE TO MEDICINE TREATMENT, ANXIETY AND DEPRESSION IN PEOPLE UNDERGOING HEMODIALYSIS TREATMENT

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ABSTRACT

Background: People with chronic kidney disease (CKD) undergoing hemodialysis may have symptoms of anxiety and depression that may interfere with adherence to medication treatment. **Objectives:** to evaluate adherence to medication use and its association with anxiety and depressive symptoms, as well as sociodemographic and clinical characteristics in people with CKD undergoing hemodialysis. **Methods:** Cross-sectional study, carried out in a hemodialysis center in a city in southwestern Goiás, Goiás, Brazil, involving 105 people with chronic kidney disease undergoing hemodialysis. The ethical aspects were met and data were collected during the months of December 2017 to January 2019, through interviews. For the outcome variables, the Morisky-Green Test and the HAD scale were used for anxiety and depression. **Results:** The overall prevalence of people adhering to the treatment was 14.3% (95%CI: 7.3-22.9%), with 70.5% having medium and low adherence. Regarding anxiety, the prevalence was 34.3% (95% CI: 25.7 – 42.9), while depression was 35.2% (95% CI: 26.7 – 44.3). There was an association between adherence to drug treatment and poor self-rated health ($p=0.001$) and anxiety ($p=0.039$); and marginal significance for depression ($p=0.054$). There was a weak negative correlation between medication adherence and anxiety ($r= -0.275$; $p=0.005$). Gender ($p=0.014$), self-rated health ($p=0.016$), and DM ($p=0.020$) were independently associated with depression. **Conclusions:** The need for multidimensional care for people on hemodialysis during care is reported, highlighting the low adherence to drug treatment and the presence of anxiety and depression, seeking to improve the quality of life of these people.

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INTRODUCTION

The evolution of chronic degenerative diseases is silent and its clinical manifestations appear after long periods of exposure to risk factors. However, care and control are essential to stop its progression. With the increase in non-communicable chronic diseases (NCDs), kidney disease represents one of the greatest challenges for public health, affecting the quality of life of many people (FASSBINDER et al., 2015). Chronic kidney disease (CKD) is a public health problem, with a progressive course and high costs, which requires specialized care resources, in addition to presenting a high morbidity and mortality. In this perspective, and according to a survey carried out in Brazil, there was an increase in the incidence and

prevalence rates regarding the number of people with chronic kidney disease, also called End-stage Renal Disease (ESRD), and undergoing hemodialysis treatment (Neves, 2020). This scenario entails challenges for family members and the exposed individual, and requires joint prevention and support actions by managers, as this problem may be associated with a worsening in quality of life and associated with anxiety and depressive symptoms (Guney, 2012; Avendaño, 2016; Shirazian, 2017; Alosaimi, 2016; Huertas-Vieco, 2014). Monitoring and treatment are key factors in reducing morbidity and mortality. Therefore, drug therapy is necessary as an adjuvant in the main treatment modality. In this scenario, it is highlighted that non-adherence to the prescribed treatment,

associated with anxiety and depression, can worsen the prognosis, having implications for the quality of life, the survival of patients and the economic cost of their treatment (Huertas-Vieco, 2014). Studies in Brazil (Oliveira, 2019; Lins, 2019; Stasiak, 2014) and in other countries¹¹⁻¹³ seek to analyze these phenomena under socioeconomic and clinical aspects, however, they point out that the research scenarios presented different and heterogeneous cuts and thus, the realization of new research in different regions of each country, need be promoted. Scientific evidence demonstrates that non-adherence to drug treatment in long-term therapies is a worldwide problem of significant magnitude, in addition to being a phenomenon of a complex nature (Clark *et al.*, 2014). Although it is evident that a range of factors can interfere with treatment adherence in people with ESRD, the prevalence varies heterogeneously, from 12.5% to 98.6% according to a systematic review study (Ghimire, 2015). Non-adherence to treatment includes multifactorial and difficult-to-control aspects, and when associated with depression and anxiety, which are common diseases in people with ESRD, it requires management procedures as early as possible, always seeking early diagnosis, which must be associated to a treatment and that impact on a better quality of life for these people (Ravaghi, 2017; Oliveira, 2016). In this perspective, it is necessary to expand the identification of the characteristics of treatment adherence in people with ESRD and the factors that influence psychosocial and socioeconomic behaviors, including anxiety and depression, and with this direction, support the management of the disease from assertive behaviors and based on the diagnostic results identified in each population. Given the above, we aim to assess adherence to medication use and its association with anxiety and depressive symptoms, as well as sociodemographic and clinical characteristics in people with ESRD undergoing hemodialysis.

METHODS

It is a cross-sectional research, with a quantitative and analytical approach, developed in a care center specialized in nephrology, located in southwest Goiás, Jataí, Goiás, Brazil. The referred hemodialysis service center includes a multidisciplinary and specialized team, serving the population of several neighboring municipalities in three work shifts, developing care for people with ESRD both from the Unified Health System, as well as from private health care. The sample consisted of people with ESRD, undergoing regular hemodialysis treatment for at least six months, regardless of gender, aged 18 years old or older and with no medical diagnosis of cognitive and psychological disorders. Exclusion criteria were: decompensation of the clinical condition during data collection, hospitalization in the last 30 days, use of antidepressants, transplant patients, and those who did not verbalize responses at the time of data collection due to limitations in cognitive conditions. Considering non-probabilistic and sequential sampling, per session shift in hemodialysis, data collection was carried out from December 2017 to December 2018, after signing the Informed Consent Form. The participants included in the study were evaluated for general characteristics, based on an instrument developed by the researchers themselves, evaluated and approved by three specialists in nephrology, containing sociodemographic and clinical variables (gender, age, marital status, skin color, education, occupation, income, self-rated health and clinical aspects).

In addition, to assess adherence to drug treatment, the Test of Morisky-Green (TMG) (Bem, 2012) was used, and the Hospital Anxiety and Depression Scale (HADS) (Transtornos do humor em enfermagem de clínica médica e validação de escala de medida, 1995) to assess the presence of anxiety and depression symptoms. For the outcome, adherence to pharmacological treatment, considering the report of people with ESRD in front of at least one positive answer among the four questions of the Morisky-Green test, we referred that a score of zero indicated high adherence, from one to two, moderate and from three to four, low adherence (Bem, 2012). The Hospital Anxiety and Depression Scale – HADS has fourteen items, seven of which correspond to depression (HADS-A) and seven to anxiety (HAD-D), whose results were dichotomized according to scoring criteria between < 8 and ≥ 8 . The application of data collection instruments was developed during the hemodialysis service, previously scheduled in the specialized unit. From a total of 140 patients in attendance at the clinic, 105 participated in the survey by signing the Informed Consent Form. The project was approved by the Research Ethics Committee of the Federal University of Goiás, under protocol number 2,284,879.

From the listed data, the analysis was carried out in the Statistical Package for Social Sciences (SPSS), version 23.0. Initially, data distribution was evaluated with normality tests and categorical variables were presented in absolute and relative frequencies and continuous variables, such as means and standard deviation. Then, univariate analysis was performed using the Chi-square and/or Fisher's exact test to assess the difference in proportions, considering the p value < 0.05 as statistically significant, to estimate the association between the outcomes (adherence to drug treatment¹⁷ and anxiety and depression, and their relationship with other independent variables, represented by socio-demographic and clinical data. In addition, Spearman correlation analyses were performed to verify the relationship between adherence scores and quantitative and for the same outcomes, it is reported that the prevalence rates were calculated with a 95% confidence interval (CI: 95%).

RESULTS

Out of the 130 patients undergoing hemodialysis, 105 (81%) were included in the study because they met the selection criteria. Thus, of the total number of patients, the prevalence of participants adhering to the treatment was 14.3% (95% CI: 7.3-22.9%). Regarding anxiety, the prevalence was 34.3% (95% CI: 25.7 – 42.9), while depression was 35.2% (95% CI: 26.7 – 44.3). Table 1 presents the TMG results in people with ESRD. Of the total, more than half (53.4%) reported that they had ever forgotten or were careless with the timetable (58.1%) when taking the drugs recommended for complementary treatment, however, on the other hand, 84.8% reported that they received information about the importance and benefit of taking oral treatment. The most recurrent reason, 58.1%, is carelessness with the time to take medication. The data presented in Table 2 describe the relation between medication adherence in people with ESRD and socioeconomic and clinical variables. Out of the total number of people with ESRD, 51.4% were male, with a mean age of 55.18 ± 1.65 , 72.4% did not perform physical activity, the majority, 85.7% deny being a smoker and 98, 1% say they are not a drinker.

Table 1. Frequency of responses to the Morisky-Green Test in people with chronic kidney disease undergoing hemodialysis, southwest region, Goiás, Brazil, 2018

Items of <i>Morisky-Green Test</i>	Yes	
	n	%
Have you ever forgotten to take your medication?	55	53.4
Have you ever been careless with your medication schedule?	61	58.1
Have you ever stopped taking medication for your illness because you felt better?	32	30.5
Have you ever stopped taking medication for your illness after feeling worse?	33	31.4
Knowledge and Motivation Item		
Have you been informed about the importance and benefit of using the drug?	89	84.8
Do you forget to replace your medications before they run out?	35	33.3

Table 2. Adherence to drug treatment using the Morisky-Green test with socioeconomic and clinical variables in people with ESRD, Goiás, Brazil, 2018

Variables	Total n (%)	Low adhesion n (%)	Medium adhesion n (%)	High adhesion n (%)	p*
Gender					0.215
Male	54 (51.4)	19 (35.2)	26 (48.1)	9 (16.7)	
Female	51 (48.6)	12 (23.5)	24 (47.1)	15 (29.4)	
Age 55,18±1,65					0.641
18-59	58 (55.2)	16 (27.6)	30 (51.7)	12 (20.7)	
≥ 60	47 (44.8)	15 (31.9)	20 (42.6)	12 (25.5)	
Shift					0.487
Morning	41 (39.0)	15 (36.6)	18 (43.9)	8 (19.5)	
Afternoon	33 (31.4)	9 (27.3)	14 (42.4)	10 (30.3)	
Night	31 (29.5)				
Days/week					0.346
Mon/Wed/Fri	60 (57.1)	21 (35)	27 (45)	12 (20)	
Tue/Thu/Sat	45 (42.9)	10 (22.2)	23 (51.1)	12 (26.7)	
Marital status					0.566
Single/Divorced/Widowed	40 (38.1)	12 (30)	21 (52.5)	7 (17.5)	
Married	65 (61.9)	19 (29.2)	29 (44.6)	17 (26.2)	
Education					0.892
< 8	71 (67.6)	22 (31)	33 (46.5)	16 (22.5)	
≥ 9	10 (9.50)	9 (26.5)	17 (50)	8 (23.5)	
Occupation					0.834
Retired/Assistance. Illness	84 (80,0)	26 (31)	40 (47.6)	18 (21.4)	
Unemployed	12 (11.4)	2 (16.7)	6 (50)	4 (33.3)	
Employed	9 (8.60)	3 (33.3)	4 (44.4)	2 (22.2)	
Income (MW)					0.872
≤ 1	68 (64.6)	20 (30.3)	32 (48.5)	14 (21.2)	
≥ 2	31 (29.5)	11 (28.2)	18 (46.2)	10 (25.6)	
Lives with					0.363
Family	17 (16.2)	24 (27.3)	42 (47.7)	22 (25)	
Alone	88 (83.8)	7 (41.2)	8 (47.1)	2 (11.8)	
Health self-evaluation					0.001
Good	45 (42.9)	6 (13.3)	30 (66.7)	9 (20)	
Bad	60 (57.1)	25 (41.7)	20 (33.3)	15 (25)	
Physical activity					0.871
Yes	29 (27.6)	8 (27.6)	15 (51.7)	6 (20.7)	
No	76 (72.4)	23 (30.3)	35 (46.1)	18 (23.7)	
Smoking					0.891
Yes	15 (14.3)	4 (26.7)	8 (53.3)	3 (20)	
No	90 (85.7)	27 (30)	42 (46.7)	21 (23.3)	
Alcoholism					-
Yes	4 (3.80)	2 (50)	2 (50)	-	
No	101 (96.2)	29 (28.7)	48 (47.5)	24 (23.8)	
Diabetes Mellitus					0.456
Yes	41 (39.0)	11 (26.8)	18 (43.9)	12 (29.3)	
No	64 (61.0)	20 (31.3)	32 (50)	12 (18.8)	
Depression					0.054
Yes	59 (56.2)	12 (20.3)	33 (55.9)	14 (23.7)	
No	46 (43.8)	19 (41.3)	17 (37)	10 (21.7)	
Anxiety					0.039
Yes	69 (65.7)	15 (21.7)	35 (50.7)	19 (27.5)	
No	36 (34.3)	16 (44.4)	15 (41.7)	5 (13.9)	
Dialysis time (years)					0.741
0 - 3	52 (49.5)	17 (32.7)	23 (44.2)	12 (23.1)	
> 3	53 (50.5)	14 (26.4)	27 (50.9)	12 (22.6)	
Sleep (hours)					0.995
≤ 5 hours	31 (29.50)	9 (29)	15 (48.5)	7 (22.6)	
> 5 hours	74 (70.50)	22 (29.7)	35 (47.3)	17 (23)	

*Bivariate analysis using Pearson's chi-square test or Fisher's exact test.

Table 3. Correlation analysis between medication adherence in pharmacological treatment and psychosocial factors in people with chronic kidney disease on hemodialysis, southwest region, Goiás, Brazil, 2018

Variables	Adhesion to medications	
	r*	p*
Depression	-0.086	0.381
Age	0.070	0.476
Anxiety	-0.275	0.005
Education (years)	-0.003	0.977
Income (minimum wage)	0.094	0.340
Dialysis time (years)	0.002	0.982
PAS	-0.149	0.130
PAD	-0.095	0.336

*Spearman's coefficient, $p < 0.05$.**Table 4. Prevalence of associated anxiety and depression symptoms among people with ESRD and socioeconomic and clinical variables, Jataí, Goiás, Brazil, 2018**

Variables	HADS-D < 8	HADS-D ≥ 8	p	HADS-A < 8	HADS-A ≥ 8	p
Gender			0.014			0.069
Female	27 (52.9)	24 (47.1)		29 (56.9)	22 (43.1)	
Male	41 (75.9)	13 (24.1)		40 (74.1)	14 (25.9)	
Health self-evaluation			0.016			0.066
Good	35 (77.8)	10 (22.2)		34 (75.6)	11 (24.4)	
Bad	33 (55.0)	27 (45)		35 (58.3)	25 (41.7)	
Days/Week			0.238			0.066
Mon/Wed/Fri	36 (60.0)	24 (40)		35 (58.3)	25 (41.7)	
Tue/Thu/Sat	32 (71.1)	13 (28.9)		34 (75.6)	11 (24.4)	
Physical activity			0.054			0.070
Yes	23 (79.3)	6 (20.7)		23 (79.3)	6 (20.7)	
No	45 (59.2)	31 (40.8)		46 (60.5)	30 (39.5)	
DM			0.020			0.981
Yes	21 (51.2)	20 (48.8)		27 (65.9)	14 (34.1)	
No	47 (73.4)	17 (26.6)		42 (65.6)	22 (34.4)	

*Bivariate analysis using Pearson's chi-square test or Fisher's exact test.

Table 5. Correlation analysis. Adherence to medications in pharmacological treatment and psychosocial factors in people with chronic kidney disease on hemodialysis, southwest region, Goiás, Brazil, 2018

Variables	HADS-D		HADS-A	
	r*	p#	r	p
Age	0.149	0.130	0.011	0.911
Education (years)	-0.078	0.430	-0.067	0.498
Income (Minimum wage)	0.002	0.985	-0.017	0.862
Dialysis time	0.003	0.976	0.066	0.503
PAS	0.032	0.747	0.069	0.489
PAD	0.071	0.473	0.050	0.615

*Spearman correlation analysis. # $p < 0.05$.

As for comorbidities, there was a prevalence of 87.6% of people with (Systemic Arterial Hypertension) SAH, 39% with DM and 41% with a history of some cardiovascular disease (CVD), 67.7% had low education, i.e., less than eight years of studies and about 80% received sick pay. Self-rated health and anxiety were statistically associated ($p < 0.005$) in the bivariate analysis. As for the depression variable, we identified a marginal association with the outcome. In this study, we present the correlation analysis in relation to adherence of patients with ESRD in relation to continuous variables. Table 3 shows a weak negative correlation with marginal significance between adherence to drug treatment and anxiety ($r = -0.275$, $p = 0.005$). Regarding symptoms of anxiety and depression, we can see in table 4 the variables that were statistically associated. Thus, we have sex ($p = 0.014$), self-rated health ($p = 0.016$), and having DM ($p = 0.020$) was independently associated with depression. However, many variables had marginal significance, which we reported, physical activity with depression ($p = 0.054$); anxiety with sex ($p = 0.069$), self-rated health ($p = 0.066$), days of the week ($p = 0.066$) and physical activity (0.070).

Table 5 shows the correlation analysis for depression and anxiety. No statistically significant results were identified in this inference.

DISCUSSION

This survey presents the first data on people with ESRD, prevalence of adherence to drug treatment, anxiety and depression, from the southwest region II of the state of Goiás, Central-West, Brazil. The low prevalence of adherence to drug treatment and the concomitant symptoms of anxiety and depression are highlighted. As for the classification of adherence, from the TMG, it was found that the main reason for low adherence in 58.1% of people was carelessness with the schedule or forgetfulness in 53.4%. Thus, analyzing the patients' responses regarding medication adherence, it was possible to identify results similar to those performed in a nephrology service of a university hospital, in which, for 35.7% of the participants, the main reason was forgetfulness and, in 27.7% carelessness with schedules (Neves, 2020).

Considering that people with ESRD are part of long-term therapy treatments and this clinical condition implies a complex, dynamic process that requires changes in their daily lives, many variables can negatively impact treatment adherence (Lins, 2019; Dantas, 2020; Alves, 2018; Santos, 2020). Furthermore and beyond these issues related to long-term therapy, it is reported that there are different methods of measuring adherence in the literature, as well as different prevalence rates in Brazil (Alves, 2018; Santos, 2020) and in other countries²⁴⁻²⁶. In this perspective, it is necessary to be careful when comparing the results of each study. In this sense, in a study carried out in two hemodialysis centers in Rio de Janeiro, adherence was assessed in four dimensions from the aspect of diet, hemodialysis, fluid restriction and among them the use of medications, but the data collection instrument used was different from this research and thus, the authors revealed high rates of adherence to drug treatment, in the amount of 93.6%⁹. Similar results and above 90% were also identified in people from a service center in the State of Bahia, where the authors described a 93.3% adherence to the use of medication (Santos, 2020). However, in a service center in the state of Minas Gerais (Alves, 2018) and in another one in Rio Grande do Sul, (2019) low prevalence was also identified, around 50.3% and 55.4%, respectively, regarding adherence to the use of medication (Alves, 2018). In this sense, we identified a variety of methodological criteria and measurement instrument both for the outcome of adherence to medications in use, as well as for anxiety and depression, which requires careful comparisons with other research scenarios. Considering the increase over the years in the incidence and prevalence rates of people on dialysis in the country, according to Brazilian survey data from several hemodialysis centers, it is important that the health team implement multidimensional care for these patients with encouragement of adherence the use of medicines and the mental health of these people. In this investigation, the predominance of men, low education, retirees, having DM and SAH as associated comorbidities, represent data similar to that of the epidemiological survey carried out in Brazil². In a systematic review, the most common factors associated with non-adherence were identified: younger age, non-white ethnicity, disease that interferes with family life, being a smoker, living single and being divorced or widowed¹⁴. Some findings were different from those found in this study when compared to the results of this systematic review, highlighting the low number of smokers and age groups of middle-aged and elderly people. However, there were similar results related to living alone and having other comorbidities, especially DM and SAH (Ghimire, 2015). Considering the health profile of people with ESRD, many challenges pervade during the long-term treatment, it is often expected that these people take responsibility for many aspects of their treatment to successfully control this chronic condition. Motivating factors for better treatment adherence such as family support, hope for kidney transplantation, improved quality of life were identified; however, barriers such as low income and aspects of long-term treatment were also revealed (Mukakarangwa, 2020).

According to the World Health Organization, there are five dimensions of adherence to long-term therapy and they are related to the health system, social and economic factors, health condition, and factors related to therapy and to the patient (World Health Organization, 2003). The association of these factors with anxiety and depression exposes people with ESRD.

The results of this study revealed that adherence to drug treatment was associated with anxiety and depression. The variable depression was associated with gender, poor health self-assessment and having DM. Depression is a frequent disorder in people with ESRD (Andrade, 2015) and may result from behavioral and biological aspects and has been associated with a worsening in quality of life and increased mortality (Shirazian, 2017). In a systematic review of studies carried out in Iran between 2003 and 2014 in people with depression, rates between 9% and 95%¹⁵ were identified and the authors highlight the inherent differences in the assessment methods and the greater use of the instrument called the Beck Inventory in the studies. The prevalence in another study in people from the same country revealed rates of 31.5% for depression and 41.7% for anxiety²⁹. In another study, carried out in Saudi Arabia, 24.6% of participants had associated depression in the elderly people, while 19.7% with anxiety symptoms was more prevalent in women (Mosleh). In Brazilian studies carried out in the state of Minas Gerais, in which they used instruments different from those used in our research, the authors identified a prevalence of 34% for depression and 32% for stress (Santos, 2017) and 41.7% for anxiety and 32.3% for depression (Brito, 2019).

Although it is evident that people with ESRD often present with depression, few are treated with either antidepressants or non-pharmacological therapy³¹. Similarly to our study, another national survey in the State of Rio Grande do Sul confirmed a high prevalence of depressive symptoms in male, retired and low-educated participants (Pretto, 2020). All these studies highlight the importance of early diagnosis and treatment initiation in improving the quality of life of exposed people. The present sample revealed a weak inverse correlation between medication adherence and anxiety, corroborating studies that report that anxiety disorders (Brito, 2019; Souza, 2017) can contribute to decreased treatment adherence⁷ and worsens the health of these people, as anxiety disorders have negative repercussions and can compromise the quality of life of the subjects (Cukor, 2017). Considering physical activity as an adjuvant in the improvement of people's quality of life, in this research we identified that of the participants with symptoms of anxiety and/or depression, about 40% reported not performing physical activity, and this result was marginally significant. In a recent study carried out in Brazil, all participants with signs of depression revealed that lack of physical activity was strongly associated³⁴. In a nephrology service of a university hospital in the Northeast region, 68.9% of the patients followed did not perform physical activity (Souza, 2017). In another study carried out in Brazil, the authors identified 55.1% of sedentary lifestyle (Lessa, 2018). Patients undergoing hemodialysis often have high levels of anxiety and depression, which may be associated with a reduction in daily physical activity and the ability to exercise (Zhang, 2014). Given the scenario identified in our research in which most patients did not perform physical activity and thus considering the benefits of physical activity in the prevention of various unfavorable health outcomes for exposed people, the implementation of exercise programs should become a reality in health care units of dialysis (Pretto, 2020). Although it is evident in the literature about the benefits of physical exercise and people with ESRD considering a recent meta-analysis³⁷, the associated exercise programs do improve physical function and capacity with consistent improvements in blood pressure and general health of people, however, still there is a lack of behaviors related to lifestyle change and

adherence to these healthy habits in these people's lives. In this study, concerning poor health self-assessment with prevalence in more than half of the participants, there was an association with low adherence and marginal significance with anxiety and these results were consistent with the study carried out in a national survey (Moreira, 2016). Among the limitations of the study, there is the use of only one indicator to assess anxiety and depression and the nature of the cross-sectional design of the study, which prevents extrapolating the outcome variables that are determinant for medication adherence or anxiety and depression. Thus, we conclude that a high number of people with ESRD do not unintentionally adhere to the recommended drug treatment. Low adherence to treatment was associated with the coexistence of symptoms of anxiety and depression, poor health self-assessment and comorbidities, including hypertension, diabetes mellitus and other cardiovascular diseases. The low prevalence of adherence to drug therapy, symptoms of anxiety and depression are relevant aspects in patients undergoing hemodialysis identified in this study, and thus, the implementation of improvements that can affect the multidimensional health of these people is a necessity. The management of actions that result in better therapeutic adherence should emerge in the different institutional settings that care for people with ESRD. However, it can be concluded that the need for multidimensional and interdisciplinary care requires the use of educational measures, with the purpose of increasing pharmacological adherence, believing that promotion actions are one of the viable strategies to achieve this goal, ensuring greater satisfaction with health and reduction of acute and chronic complications. It reports the need to institute permanent interdisciplinary education strategies that can contribute to an improvement in health care for these people.

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