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Patients on chemotherapy: depression and adherence to treatment

PACIENTES EM USO DE QUIMIOTERÁPICOS: DEPRESSÃO E ADESÃO AO TRATAMENTO

PACIENTES EN USO DE QUIMIOTERÁPICOS: DEPRESIÓN Y ADHESIÓN AL TRATAMIENTO

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ABSTRACT

This analytical, cross-sectional study applied a quantitative approach to verify the presence of depression and the adherence to a chemotherapy treatment in patients with cancer at the central chemotherapy pharmacy of a university hospital. The sample consisted of 102 patients, and data were collected from October 2010 to May 2011. A structured interview was used to obtain sociodemographic, clinical and therapeutic data; the Morisky Test and Beck Depression Inventory were also applied. The results revealed that 10.8% and 1.9% of participants had moderate and severe depression, respectively. The presence of depression was significantly associated with variables such as income per capita, the number of surgeries, and disease duration. A lack of treatment adherence was identified in 48% of participants. These results indicate the need for health staff training to detect depressive disorders and chemotherapy treatment attrition among patients with cancer.

DESCRIPTORS

Drug therapy
Depression
Medication adherence
Patient care team
Oncologic nursing

RESUMO

Este trabalho trata-se de estudo analítico, transversal, com abordagem quantitativa, que verificou a presença de depressão e a adesão ao tratamento com quimioterápicos em pacientes oncológicos atendidos na Farmácia Central de Quimioterapia de um hospital universitário. A amostra constou de 102 pacientes e a coleta dos dados foi realizada no período de outubro de 2010 a maio de 2011. Utilizou-se a entrevista estruturada, norteada por roteiro contendo dados sociodemográficos, clínicos e terapêuticos; o Teste de Morisky e o Inventário de Depressão de Beck. Os resultados revelaram que 10,8% e 1,9% dos participantes apresentaram depressão moderada e grave, respectivamente. Houve associação estatisticamente significativa entre a presença de depressão e as variáveis renda per capita, número de cirurgias e tempo de doença. Identificou-se falta de adesão ao tratamento em 48% dos participantes. Tais resultados indicam a necessidade de treinamento da equipe de saúde para detectar transtornos depressivos e falta de adesão ao tratamento com quimioterápicos entre pacientes oncológicos.

DESCRITORES

Quimioterapia
Depressão
Adesão à medicação
Equipe de assistência ao paciente
Enfermagem oncológica

RESUMEN

Estudio analítico, transversal, cuantitativo, verificando la presencia de depresión y adhesión al tratamiento con quimioterápicos en pacientes oncológicos atendidos en la Farmacia Central de Quimioterapia de un hospital universitario. Muestra constituida por 102 pacientes, datos recolectados de octubre 2010 a mayo 2011. Se utilizó entrevista semiestructurada, orientada por rutina conteniendo datos sociodemográficos, clínicos y terapéuticos; el Test de Morisky y el Inventario de Depresión de Beck. Los resultados expresaron que 10,8% y 1,9% de los participantes presentaron depresión moderada y grave, respectivamente. Existió asociación estadísticamente significativa entre presencia de depresión y las variables renta per cápita, número de cirugías y tiempo de la enfermedad. Se identificó falta de adhesión al tratamiento en 48% de los participantes. Tales resultados indican la necesidad de capacitación del equipo de salud para detectar transtornos depresivos y falta de adhesión al tratamiento con quimioterápicos en pacientes oncológicos.

DESCRIPTORES

Quimioterapia
Depresión
Cumplimiento de la medicación
Grupo de atención al paciente
Enfermería oncológica

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INTRODUCTION

Cancer is a stigmatized disease because it causes suffering and triggers many changes in the lives of people. The high incidence of cancer makes these issues even more concerning. According to the report of the International Agency for Research on Cancer (IARC)[1], the global impact of cancer more than doubled over the last 30 years. Approximately 12 million new cases of the disease occurred in 2008, with seven million deaths. Continuous population growth and aging significantly affects the incidence and effect of cancer throughout the world. Countries with low and medium levels of development were particularly affected; the IARC estimated that half of the new cases and approximately two-thirds of the deaths caused by cancer in 2008 occurred in these countries[1].

After a cancer diagnosis is disclosed, the physical and psychological changes that are triggered by cancer are evident and have significant effects, leading primarily to anxiety and depression[2]. These psychological conditions often persist throughout treatment and may be related to the treatment's side effects. Hair loss, vomiting and various bodily changes are frequent, and even when these effects are temporary, they may contribute to depression.

Depression is an important disease and deserves attention. It is a common mental disorder whose primary symptoms include a depressed mood, loss of interest or pleasure, feelings of guilt, low self-esteem, sleep and eating disorders, and a loss of energy and concentration. These problems may become chronic or recurrent and substantially harm one's ability to perform daily responsibilities. One study found that patients with cancer, pain, and depression are at risk for suicide[3].

Depression is common among patients with cancer[4]. Although this psychiatric disorder is recurrent in this population, depression is often overlooked or improperly treated. Patients with cancer tend not to discuss depressive symptoms, and oncologists tend not to ask about them. These behaviors might be related to the patient belief that they must appear strong so that the physician will not withdraw treatment or the oncologist belief that patients will discuss depression of their own volition when they experience it[5].

The difficulty in diagnosing depression might be because both depression and cancer present common symptoms such as a depressed mood, a lack of pleasure, fatigue, and weight loss. In addition, the clinical staff might underestimate depressive symptoms because they expect patients with cancer to be depressed[3].

Patient adherence to medication is as important as correctly diagnosing depression and other symptoms. However, treatment adherence might be lower among patients with cancer, especially those who are depressed, because depression results in physical and emotional impairment in addition to reduced self-care, which decreases patient prognoses[3].

Adherence is the degree of agreement between the individual's behavior and the recommendations of the physician or another health worker. Multiple factors influence adherence [6].

The literature reports that the duration of the treatment partially explains low adherence because following a treatment regularly is often difficult [7]. Other factors also influence adherence such as the healthcare system, the delivery of services, the disease and the treatment itself. Unfortunately, low adherence is the primary cause of a decreased clinical condition, and health workers often ignore this problem. This factor is relevant because depression can increase the risk of relapse after treatment and reduce adherence to anticancer therapies[8].

Because the aforementioned aspects indicate that depression might be present among patients with cancer, and this pathology affects treatment adherence, the progress of the cancer and the patient's quality of life, this study sought to verify adherence to a chemical therapy and the signs of depression.

Patients with cancer tend not to discuss depressive symptoms, and oncologists tend not to ask about them.

METHODS

This analytical, cross-sectional study applied a quantitative approach and was conducted in the pharmacy of the chemotherapy center at a large university hospital located in a city in the state of São Paulo, Brazil. This pharmacy distributes oral and injectable chemotherapy medications free of cost to the patients who are cared for at the facility.

The sample was composed of 102 patients with cancer who attended the chemotherapy center pharmacy and received medication from October 2010 to May 2011. The inclusion criteria were having a diagnosis of cancer; a prescription for chemotherapy medication or non-chemotherapy medication to treat cancer; and aged 18 years or older.

Data were collected using a structured interview that was guided by a script composed of three sections. The first section addressed patient demographic, socioeconomic, clinical and therapeutic data. The medication description was based on the Anatomical Therapeutic Chemical (ATC) first level provided by the WHO (*www.whocc.no/atc_ddd_index*).

The second section of the script was designed to identify the adherence to chemotherapy treatment using the Morisky test[9]. This instrument is used to identify patient level of adherence to medication and evaluates

the behavior of patients with regard to their daily medication use. Four questions comprise this test: *Have you ever forgotten to take your medicine?*; *At times, are you careless about taking your medicine?*; *Do you sometimes stop taking your medicine when you feel better?*; and *Do you sometimes stop taking your medicine when it causes you to feel worse afterwards?*

Adherence was assessed with *Yes* and *No* answers to which values of 0 and 1 were assigned, respectively. A criterion to classify adherence level was used to compare and discuss the results in this study: Those with zero points were considered to have *greater adherence*, whereas those who obtained one to four points were considered to have *less adherence*.

The Beck Depression Inventory was used[10] in the third section of the script. This survey was designed to identify the presence of depression symptoms in the sample. This self-report symptomatic scale is composed of 21 items with answers that address the individual's condition and correspond to the different levels of depression. The sum of the individual item scores provided a total dimensional score of depression intensity that can be classified as minimum, mild, moderate or severe. The choice of an appropriate cutoff point depends on the nature of the sample and the study objectives. Scores above 15 might detect dysphoria among non-diagnosed samples such as the current study, whereas scores above 20 points denote *depression*.

After the instruments were applied, the adherence and Beck Depression Inventory data were stored in a database spreadsheet and then analyzed using the public domain program EpiInfo™, Version 3.2 (*http://www.cdc.gov/epiinfo*). The potential association between the dependent and independent variables was verified using Fisher's Exact Test. Thus, the variables were dichotomized, and the significance threshold was fixed at $p<0.05$.

This study has methodological limitations: It is a convenience sample composed of patients with different types of cancer and includes a greater percentage of patients with breast cancer than other types of cancer. In addition, this sample was composed of outpatients from a specialized public service, which limits the generalization of results.

The facility's Ethics Research Committee (Process HCRP No. 6349/2010) approved this project, and the participants signed informed consent forms in accordance with Resolution 196/96, the Brazilian National Council of Health.

RESULTS

Most of the 102 interviewees were women (82.4%) who were married (52.9%) and retired (34.3%) or homemakers (25.5%). The sample ranged in age from 25 to 87 years old. Table 1 shows that most patients who underwent treatment used one chemotherapy medication (90.2%), and usually that medication belonged to the classification L02B (hormone agonists and related agents; 61.2%). A majority of patients had already undergone at least one surgery (64.7%). One patient had undergone seven surgeries, which was the highest number of surgeries reported.

Table 1 - Distribution of participants according to the clinical and therapeutic variables, Ribeirão Preto, SP, Brazil 2011

Variable	N	%
Number of medications		
1 medication	92	90.2
More than 1 medication	10	9.8
ATC Classification		
Alkylating agents (L01A)	05	4.3
Antimetabolites (L01B)	13	11.2
Plant alkaloids and other natural products (L01C)	04	3.4
Cytotoxic antibiotics and related substances (L01D)	03	2.6
Other antineoplastic agents (L01X)	17	14.7
Hormones and related agents (L02A)	03	2.6
Hormonal agonist and related agents (L02B)	71	61.2
Primary Diagnosis		
Stomach	01	1.0
Liver	01	1.0
Intestine	11	10.8
Lymphatic	02	2.0
Breast	70	68.6
Medullary origin	13	12.7
Prostate	04	3.9
Number of surgeries		
Up to 1 surgery	66	64.7
More than 1 surgery	36	35.3
Time since diagnosis		
1 - 36 months	51	50.0
36 -144 months	51	50.0
Total	102	100

We observed that 10.8% and 1.9% of the participants presented moderate or severe forms of depression, respectively. Table 2 shows the significant associations with the levels of depression and *per capita* income ($p=0.0455$), the number of surgeries ($p=0.0324$), and the duration of disease ($p=0.0149$). A higher percentage of depression was observed among patients who had a monthly income of no more than 329 Brazilian reals (21.6%), had undergone two or more surgeries (25%), and experienced the disease for up to 36 months (24.2%).

Although Fisher's exact test did not reveal a significant association for the remaining variables, certain relevant aspects were observed such as a greater percentage of depression among men (22.2%) compared with women (13.1%), among those who completed primary school (16.1%) compared with those who had a college or postgraduate education (6.7%), and among those who used more than one medication (20.0%).

Given that antidepressants are generally prescribed for patients with moderate or severe depression, we opted to divide the participants into two groups: *no depression and mild depression* and *moderate and severe depression* to present data by medication use. We found that 5.9% of patients with moderate or severe depression did not use antidepressants, whereas 8.8% of patients used medication but still presented depressive symptoms according to the Beck Inventory. We noted that 8.8% of the patients who did not show depression or mild depression used antidepressants.

Table 2 - The prevalence of depression by the demographic, socioeconomic, clinical and therapeutic variables, Ribeirão Preto, SP, Brazil 2011

Variable	Dysphoria and no depression	Moderate and severe depression	Total	P
	N(%)	N(%)	N(%)	
Idade				
Below 55 years of age	45 (84.9)	08 (15.1)	53 (100.0)	0.5660
Above 56 years of age	42 (85.7)	07 (14.3)	49 (100.0)	
Gender				
Male	14 (77.8)	04 (22.2)	18 (100.0)	0.2549
Female	73 (86.9)	11 (13.1)	84 (100.0)	
Marital status				
Partner	46 (85.2)	08 (14.8)	54 (100.0)	0.4888
No partner	41 (85.4)	07 (14.6)	48 (100.0)	
Schooling				
Complete primary school	73 (83.9)	14 (16.1)	87 (100.0)	0.3080
College or postgraduate	14 (93.3)	01 (6.7)	15 (100.0)	
Occupation				
Employment	61 (85.9)	10 (14.1)	71 (100.0)	0.5025
No income	26 (83.9)	05 (16.1)	31 (100.0)	
Income *Per Capita*				
Up to 329 reals	40 (78.4)	11 (21.6)	51 (100.0)	0.0455*
More than 329 reals	47 (92.2)	04 (7.8)	51 (100.0)	
Number of dependents				
Up to 3 dependents	67 (87.0)	10 (13.0)	77 (100.0)	0.2870
More than 3 dependents	20 (80.0)	05 (20.0)	25 (100.0)	
Number of surgeries				
Up to 1 surgery	60 (90.9)	06 (9.1)	66 (100.0)	0.0324*
More than 2 surgeries	27 (75.0)	09 (25.0)	36 (100.0)	
Number of medications				
Up to 1 medication	79 (85.9)	13 (14.1)	92 (100.0)	0.4509
More than 1 medication	08 (80.0)	02 (20.0)	10 (100.0)	
Duration of disease				
Up to 36 months	47 (75.8)	15 (24.2)	62 (100.0)	0.0149*
More than 36 months	40 (95.2)	02 (4.8)	42 (100.0)	

*Significant

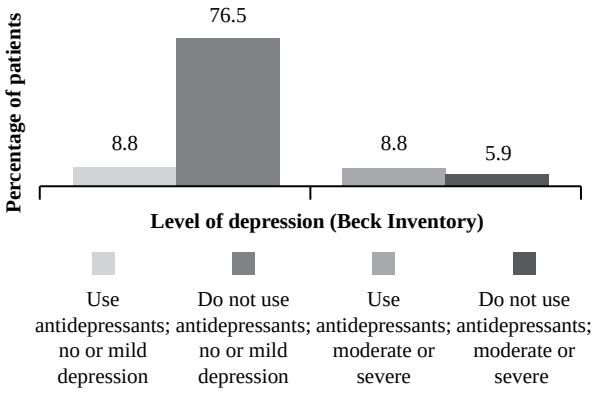

Figure 1. The distribution of participants by level of depression and use of antidepressants

Forty-eight percent of patients did not adhere to the chemotherapy treatment, as shown in Figure 2, whereas 5.9% of patients experienced moderate or severe depression.

Table 3 presents the results of Fisher's Exact test, which did not reveal a significant association between chemotherapy adherence and the studied variables ($p > 0.05$), although certain aspects should be noted.

Table 3 shows significant differences did not exist between genders ($p = 0.1319$), although the percentage of women who did not adhere to chemotherapy was higher (51.2%) than that of men (33.3%).

Most (60%) patients with a college degree or postgraduate studies did not adhere to a chemical therapy medication, whereas the adherence percentage of those who completed primary school was 54%.

We found that 51% of patients with a *per capita* income of no more than 329 reals did not adhere to their chemotherapy medication. In addition, those who underwent two or more surgeries had a higher adherence percentage (55.6%) compared with those who underwent one or no surgeries (50%). Moreover, a higher adherence percentage existed among patients who lived with the disease for more than 36 months (57.1%) compared with those who experienced the disease for a shorter period (48.3%).

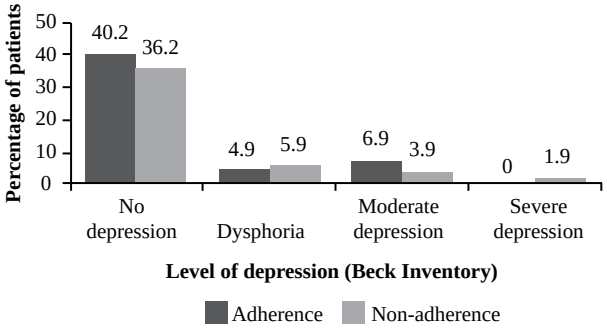

Figure 2. The distribution of participants by level of depression and adherence to chemotherapy treatment

Table 3 - The prevalence of chemotherapy treatment adherence by the demographic, socioeconomic, clinical and therapeutic variables, Ribeirão Preto, SP, Brazil 2011

Variável	Aderente	Não aderente	Total	P
	N(%)	N(%)	N(%)	
Age				
Below 55 years of age	27 (50.9)	26 (49.1)	53 (100.0)	0.4938
Above 56 years of age	26 (53.1)	23 (46.9)	49 (100.0)	
Gender				
Male	12 (66.7)	06 (33.3)	18 (100.0)	0.1319
Female	41 (48.8)	43 (51.2)	84 (100.0)	
Marital status				
Partner	29 (53.7)	25 (46.3)	54 (100.0)	0.4304
No partner	24 (50.0)	24 (50.0)	48 (100.0)	
Schooling				
Complete primary school	47 (54.0)	40 (46.0)	87 (100.0)	0.2346
College or postgraduate	06 (40.0)	09 (60.0)	15 (100.0)	
Occupation				
Employment	39 (54.9)	32 (45.1)	71 (100.0)	0.2442
No income	14 (45.2)	17 (54.8)	31(100.0)	
Income *Per Capita*				
Up to 329 reals	25 (49.0)	26 (51.0)	51 (100.0)	0.3460
More than 329 reals	28 (54.9)	23 (45.1)	51 (100.0)	
Number of dependents				
Up to 3 dependents	41 (53.2)	36 (46.8)	77 (100.0)	0.4102
More than 3 dependents	12 (48.0)	13 (52.0)	25 (100.0)	
Number of surgeries				
Up to 1 surgery	33 (50.0)	33 (50.0)	66 (100.0)	0.3713
More than 2 surgeries	20 (55.6)	16 (44.4)	36 (100.0)	
Number of medications				
1 medication	48 (52.2)	44 (47.8)	92 (100.0)	0.5782
More than 1 medication	05 (50.0)	05 (50.0)	10 (100.0)	
Duration of disease				
Up to 36 months	29 (48.3)	31 (51.7)	60 (100.0)	0.2500
More than 36 months	24 (57.1)	18 (42.9)	42 (100.0)	

DISCUSSION

Depression is an affective disorder characterized by an overall psychological and physiological alteration that changes the way individuals attribute value to reality and life. Depression affects approximately 25% of patients with cancer. The stress and emotional distress related to a diagnosis of cancer can trigger depression[11].

Clinical guidelines for screening depression are essential in the routine treatment of patients with cancer. This comorbidity significantly affects the individual's quality of life, their adherence to anticancer treatments, the length of hospitalization, health costs, morbidity and mortality[12].

In the current study, 10.8% and 1.9% of the patients with cancer taking chemotherapy medication presented moderate or severe depression, respectively. In addition to the aforementioned factors, the use of anticancer therapies such as interferon, interleukine-2, procarbazine, asparaginase, vinblastine, vincristine, tamoxifen, cyproterone, and other chemotherapeutic agents and corticosteroids (e.g., prednisone and dexamethasone) cause a depressive state. Furthermore, the depression among cancer patients might be a direct consequence of these therapies[13].

We noted that breast cancer affected 68.6% of the current sample. A study that characterized the profile of 61 patients with cancer who received oral anticancer medications also found that breast cancer was the most frequent type of cancer reported (28%)[14]. Another study addressed the associations among depressive symptoms, socio-demographic, and clinical variables in 71 women with breast cancer and found that only chemotherapy was significantly associated with depressive symptoms among the clinical variables[15]. These findings might partially explain the high rate of depression identified in this study.

Importantly, the high percentage of patients with breast cancer was also reflected in the high percentage of medication classified as L02B (hormonal agonist and related agents), which includes medication frequently used to treat this type of cancer, especially tamoxifen. This aspect is relevant because the literature shows that the use of tamoxifen or other antiestrogens presents a theoretical risk of developing depression[16].

The results revealed a significant association between the presence of moderate/severe depression and per capita income, the number of surgeries, and the duration of disease. One study of low-income women with cancer also identified a high prevalence of major depression (24%)[17]. The literature corroborates the present study's results because it indicates that the time after diagnosis and treatment is an important variable associated with the incidence of depression among patients with cancer[18].

This study also identified a high percentage of depression among patients who underwent two or more surgeries. We did not identify studies in the literature that addressed this aspect with regard to depression in patients with cancer. One hypothesis is that many surgeries generate uncertainty and even hopelessness in relationship to the prognosis; however, additional studies are required to provide more evidence.

We found that 5.9% of patients who presented moderate or severe depression did not take antidepressants, and 8.8% of those using antidepressants presented symptoms of moderate or severe depression. These findings draw attention to the possibilities that the treatment is not efficient or the patient is not adhering to it. However, the literature shows that antidepressants are effective and increase adherence to cancer treatments, and prior treatments with these medications may minimize depression among patients with cancer[4].

We noted that the decision to implement antidepressants among this clientele should be carefully considered. Psychiatric conditions including depression and anxiety negatively affect the progression of cancer and often lead to treatment abandonment. Moreover, drug interactions should be considered, especially between antidepressants and chemotherapy medications[16]; thus, oncologists and psychiatrics should interact with one another[4, 18]. The literature shows that most oncologists are unfamiliar with depressive symptoms, and mental health specialists do not frequently work with oncologists[4, 18].

This issue might contribute to a difficult diagnosis and treatment of depression among patients with cancer. As mentioned above, the obstacles to treating depression among these patients may arise due to various factors including the uncertainty regarding their diagnosis and treatment, the lack of time to investigate emotional issues, and the costs associated with treatment[13].

Forty-eight percent of the patients in this study did not adhere to chemotherapy treatment. This figure is similar to the 50% average observed among patients with chronic diseases as reported by the World Health Organization[6]. Nevertheless, this percentage is higher than the 28% observed by a study that investigated the adherence to an oral chemotherapy among patients with cancer[14]. A scarcity of studies that specifically address aspects related to treatment adherence among patients with cancer exists.

Among the patients who did not adhere to treatment, 5.8% presented moderate or severe depression. The literature reveals that depression can reduce adherence to anticancer therapies[8], in addition to affecting a patient's immunological functions, thereby reducing their chance for survival. A recent meta-analysis of 31 prospective studies found a 25% higher rate of mortality among patients with cancer with depressive symptoms[19].

In terms of the variables related to adherence, most of the patients in the current study with a duration of disease longer than 36 months adhered to the chemotherapy. These findings contradict a study that found that patients who had the disease for shorter periods felt more control over their health[14]. Nevertheless, the present study's data, which showed that patients with cancer for a less time presented a higher level of depression, might partially explain their low treatment adherence.

Another variable investigated involved the relationship between adherence to chemotherapy and socioeconomic level. The results showed that most patients with a *per capita* income of no more than 329 reals did not adhere to chemotherapy. One study investigated the influence of socioeconomic factors on the treatment of acute lymphocytic leukemia and reported that 47% of patients considered to be poor refused or abandoned chemotherapy treatment and received less individualized care from oncologists[20]. Hence, we verified that socioeconomic hardship is negatively influences adherence to cancer treatment and potentially affects disease prognosis.

These findings reveal the need to pay greater attention to patients with these characteristics as well as for health staffs to help them to develop their potential to cope with cancer and strategies that encourage medication therapy adherence. Adherence to therapy cannot be a passive attitude; that is, it cannot be an imposition to any doctor or other health worker. Such an attitude must be active, and the patient must be committed to therapy. Belief in the treatment is important, and incentives are needed to maintain this belief. Hence, a successful relationship between the patient and the health staff is essential[6].

One study[21] indicated that printed material supporting verbal recommendations facilitated effective communication between health workers and patients. When patients and caregivers are well instructed regarding the appropriate way to self-care and provide care, respectively, they feel safer thereby favoring adherence to treatment.

CONCLUSIONS

This study investigated adherence to chemotherapy treatment and the symptoms of depression among patients who attended the pharmacy in the chemotherapy center of a university hospital. In addition to the high percentage of patients with moderate or severe depression, a significant association was found between the presence of depression and *per capita* income, the number of surgeries, and the time of disease. These findings reinforce the importance of screening for depressive symptoms among patients with cancer using simple instruments and specific questions during a routine assessment.

The fact that 48% of participants did not adhere to a chemotherapy treatment drew our attention. Although a lower percentage of treatment adherence was observed among females, those with less *per capita* income, fewer surgeries, a shorter duration of disease and more education, these associations were not significant. These data suggest that other variables interfere with adherence to chemotherapy treatment, which demonstrates a need for longitudinal studies to identify them.

Considering the high percentage of patients with cancer with depressive symptoms, the lack of adherence to chemotherapy treatment identified in this study, and the negative influence of these aspects on disease progression, we stress the importance of implementing strategies in health services that focus on attentive listening and establish bonds that identify depressive symptoms and non-adherence as well as provide appropriate educational and psychosocial interventions so that these patients develop the motivation needed to continue their therapy.

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