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ADHERENCE TO TREATMENT IN PATIENTS WITH SOLID AND HEMATOLOGICAL CANCERS. COULD SPIRITUAL AND PSYCHOLOGICAL SUPPORT FACILITATE OPTIMAL ADHERENCE?

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ABSTRACT – *Objective:* Cancer-related diseases pose a substantial public health challenge; however, recent treatments have enhanced patient outcomes. Adherence to therapy is crucial, and research focuses on elucidating the factors that influence it. Limited information exists on medication adherence in cancer patients. This study aims to identify risk factors for non-adherence in a cohort of people with solid and hematological tumors.

Participants and Methods: This is a cross-sectional study in which participants were recruited from two Oncologic hospital units in Italy. The inclusion criteria were age ≥ 18 years, confirmed malignant neoplasm, and active treatment. Data included sociodemographic and clinical-oncological factors. Treatment adherence was assessed through a clinician-based dichotomous scale. Health-related quality of life (HRQoL) was evaluated with the Short Form Health Survey – 12 items (SF-12), satisfaction with care was measured using the Treatment Perception Questionnaire.

Results: A total of 263 participants (132 females, 50.2%) was involved in this study. The mean age was 61.2±13.8. Non-adherence frequency was 9.9%. Factors associated with non-adherence were shorter time since care initiation (<6 months), receiving palliative care, having a solid cancer diagnosis. Non-adherence was higher in solid cancer (12.4%) compared to hematologic cancer (1.6%). In the combination of risk factors, a significant association was found between unemployment/high level of education and non-adherence.

Conclusions: The study found a low non-adherence rate to oncological treatments, possibly due to strong psychological and spiritual support. However, individuals with higher education and unemployment showed specific non-adherence risk, necessitating attention to their emotional challenges while facing cancer.

KEYWORDS: Adherence, Cancer, Risk factors, Psychological support, Spiritual support.

INTRODUCTION

Oncological diseases represent a relevant public health issue. However, in recent years, there have been notable advancements in therapies, leading to substantial improvements in the medium and long-term outcomes of many oncological conditions. In this new context, adherence to treatment has become a crucial aspect. The effectiveness of these new treatments remains hampered without the cooperation and awareness of individuals with health issues. Consequently, this topic has garnered strong scientific interest, resulting in the publication of numerous research papers, systematic reviews, and meta-analyses.

Certain contributions have examined older adults who may experience comorbidity with chronic diseases such as hypertension, type II diabetes, as well as cognitive and sensory impairments, which can negatively impact adherence[1]. The determinants of non-adherence among older adults have varied across studies, with adherence rates ranging from 52% to 100% [1]. The subject of malignancies in the elderly holds significant importance, considering that this age group faces the highest cancer risk. Moreover, the matter of non-adherence to onco-hematological treatments is equally compelling, given its implications for individuals of all age groups, including younger individuals [2,3]. Meta-analyses conducted in this field have concluded that there is a lack of valid and reliable information regarding medication adherence among hematological cancer patients [2].

One of the largest cross-sectional surveys in this area found a medication adherence prevalence of 50% among a group of approximately 300 patients. In univariate analysis, factors such as younger age, higher education level, living alone, being employed, perceiving insufficient social support, experiencing depression, and overall health were significantly associated with medication non-adherence. In the multivariable analysis, younger age, higher education level, and fatigue remained significantly associated with medication non-adherence [3]. The aim of this study is to assess the risk factors for treatment non-adherence in a large, mixed cohort of patients with solid and hematological tumors upon admission.

PARTICIPANTS AND METHODS

Study design

This cross-sectional study was built upon previous cohort study findings [4,5].

Study Sample

Participants were recruited from January 2018 to January 2020 from the Oncology Unit at the University Hospital of Cagliari, Italy and the Hematology Unit and Stem Cell Transplantation Center at Azienda Ospedaliera Brotzu, Cagliari, Italy. Inclusion criteria for cohort admission were age ≥ 18 years, any gender, histologically confirmed malignant neoplasm and active treatment.

Study tools

A customized schedule collected sociodemographic (gender, marital status, employment, education) and clinical-oncological (inpatient/outpatient status, follow-up timing, cancer diagnosis, cancer stage) data. Treatment adherence was assessed through a clinician-based dichotomous scale.

The Italian version[6] of the SF-12 (Short Form Health Survey - 12 item) [7] was used to evaluate health-related quality of life (HRQoL). The SF-12 is a self-report questionnaire that assesses two dimensions of perceived HRQoL: physical (6 item) and psychological (6 item). Higher scores correspond to better HRQoL.

The Italian version [8] of the TPQ (Treatment Perception Questionnaire) [9] was used to measure satisfaction with care. It is a 10-item self-reported questionnaire that measures two components: patients' perception of the quality of their interactions with healthcare staff (5 item) and satisfaction with the care program (5 item). The questionnaire utilizes a five-point Likert scale, with higher scores indicating greater satisfaction.

Statistical analysis

Descriptive statistics reported frequencies (percentages) and mean±standard deviation for sociodemographic and clinical-oncological variables. Chi-square tests (with Yates's correction) and one-way ANO-

VA (with Bonferroni correction) compared frequencies and means between non-adherent and adherent individuals. Multivariate analyses were conducted to assess potential interactions. Statistical significance was set at $p < 0.05$.

RESULTS

Characteristics of the study sample

A total of 263 participants (132 females, 50.2%) were recruited using non-probabilistic sampling from the Oncology Units of two agencies in Cagliari, Italy (Azienda Brotzu, Ospedale Businco, n=62, 23.6%; University Hospital of Cagliari, n=201, 76.4%). The mean age was 61.2±13.8. Among the participants, 76.4% had solid cancer, while 23.6% had blood cancer. The most common treatment objective in the cohort was palliative care (56.7%). Descriptive data can be found in Table 1.

Non-adherence to treatment and its associated factors

The association between socio-demographic and clinical factors and treatment non-adherence is presented in Table 1. The overall frequency of non-adherence was 9.9%. In univariate analysis, factors significantly associated with non-adherence were: "time since the beginning of CARE (<6 months)", OR=3.48 (95% CI 1.45-8.33); "receiving palliative care", OR=3.58 (95% CI 1.30-9.80); "having a solid cancer diagnosis" (*vs.* hematologic cancer diagnosis), OR=8.66 (95% CI 1.15-65.31). Non-adherence was observed in 25 out of 201 participants (12.4%) with solid cancers, while only 1 out of 62 participants (1.6%) with hematologic cancer showed non-adherence. Certain conditions showed associations bordering on significance, such as unemployment, the presence of depressive symptoms, and advanced cancer stage. In the combination of risk factors, a significant association was found between unemployment/high level of education and non-adherence, OR=4.22 (95% CI 1.20-14.74).

DISCUSSION

The data from this study reveal a relatively modest rate of treatment non-adherence within a sample of individuals predominantly in the older age group, presenting with solid or hematologic oncological pathologies. Factors associated with non-adherence included the time since the beginning of treatment (<6 months), receiving palliative care, having a solid cancer diagnosis compared to hematologic cancer, having a higher education level combined with unemployment status. The overall percentage of non-adherence observed in our sample is considerably lower than those reported in studies involving elderly cancer patients [1,10] and/or patients with blood cancer [3,11].

The two units involved in the study provide outpatient care with occasional short hospitalizations during critical periods or for procedures requiring close monitoring. These short hospitalizations offer patients the opportunity to undergo instrumental and laboratory tests promptly, which is significant considering the typically long waiting times for such tests in the public health system for outpatients[12]. Although satisfaction with care level did not emerge as a determinant of treatment adherence, the availability of continuous and cost-free care for patients can serve as a strong motivator for treatment continuity. It is also worth noting the provision of psychosocial and spiritual support services by both facilities. According to complementary and alternative medicine in cancer treatment [13-15], having access to psychological and spiritual care is a crucial aspect, as the absence of such support can contribute to treatment non-adherence [10]. Both examined units are located in hospitals outside the city center, which is a common characteristic of many hospitals in Europe today. These units provide on-site psychological support services and are also closely connected to an outpatient unit located in the city center of Cagliari. This outpatient unit is easily accessible by public transportation from the entire region due to its proximity to the train and bus station. This accessibility allows users to attend weekly psychotherapy sessions conveniently. Additionally, spiritual support units are available within the hospitals and open to individuals of all religious backgrounds, including religious minorities. Although not directly measured in this study, these aspects could potentially explain the low rate of non-adherence and should be considered as a heuristic hypothesis that requires further confirmation.

Table 1. Study Sample.

Variables	Overall (N=263)	Variables	Overall (N=263)
HEALTH AGENCY		**CANCER TYPE**	
Brotzu Unit	62 (23.6%)	Blood	62 (23.6%)
University Hospital Unit	201 (76.4%)	Solid	201 (76.4%)
SEX		**CANCER STAGE***	
M	131 (49.8%)	1 or 2	29 (11.0%)
F	132 (50.2%)	3 or 4	234 (89.0%)
AGE		**INTENT OF TREATMENT**	
Mean (±SD)	61.2 (±13.6)	Palliative	149 (56.6%)
MARITAL STATUS		Curative, adjuvant, support	
Single or without a partner	86 (20.9%)	or maintenance	134 (43.4%)
Married or with a partner	177 (70.1%)	**RESPONSE TO TREATMENT**	
EMPLOYMENT STATUS		Ongoing evaluation	62 (23.6%)
Employed or retired or student	238 (90.5%)	Absence of cancer	56 (21.3%)
Unemployed	25 (9.5%)	Cancer in progress	50 (19%)
EDUCATIONAL LEVEL		Not applicable	1 (0.4%)
< high school	126 (47.9%)	Partial	28 (10.6%)
> high school	137 (52.1%)	Stable	65 (24.7%)
ACCESS TO CARE		(Missing)	1 (0.4%)
Out-patient (Day Hospital)	217 (82.5%)	**ADHERENCE TO CANCER TREATMENT**	
In-patient (Hospital Ward)	46 (17.5%)	YES	237 (87.5%)
TIME since the beginning of CARE		NO	26 (9.9%)
<6 months	111 (42.2.%)		
>6-12 months	152 (57.8%)		
CANCER SITE			
Non-Hodgkin Lymphoma	13 (4.9%)		
Gastroenteric	92 (35%)		
Gynecological	32 (12.2%)		
Breast	32 (12.2%)		
Rare	9 (3.4%)		
Unknow	5 (1.9%)		
Lung	18 (6.9%)		
Uro-Genital	17 (6.5%)		
Hodgkin Lymphoma	14 (5.3%)		
Chronic Lymphocytic Leukemia	10 (3.8%)		
Immune Thrombocytopenic Purpura	2 (0.8%)		
Langerhans Cell Histiocytosis	1 (0.4%)		
Acute Myeloid Leukemia	1 (0.4%)		
Multiple Myeloma	7 (2.7%)		
Myelofibrosis	2 (0.8%)		
Chronic Myeloid Leukemia	3 (1.1%)		
Head And Neck	1 (0.4%)		
Polycythemia Vera	1 (0.4%)		
Myelodysplastic Syndrome	3 (1.1%)		

*1= unique localization in one nodal station or extra-nodal; 2= two or more localizations from the same side of the diaphragm, 3= localizations from both sides of the diaphragm; 4= diffuse disease.

Table 2. Risk factors associated with adherence to cancer treatment.

Risk factors	Not adherence to cancer treatment 26 (9.9%)	Adherence to cancer treatment 237 (90.1%)	Total N 263	χ^2 (With Yates correction), OR (95% CI) or F (df) (with Bonferroni test)	*p*
Sex (Female)	13 (50%)	119 (50.2%)	132 (50.2%)	χ^2=0.397, OR=0.79 (0.35-1.79)	0.579
Age	65.46±14.35	60.67±13.52	61.2±13.60	F (df 1,261)=2.906	0.089
Without partner (*vs.* with partner)	7 (26.9%)	79 (44.6%)	86 (32.7%)	χ^2=0.437, OR=0.73 (0.30-1.83)	0.508
Unemployed	5 (19.23%)	20 (7.6%)	25 (9.5%)	χ^2=3.172, OR=2.58 (0.88-7.59)	0.075
≥High school	12 (46.1%)	125 (52.7%)	137 (52.1%)	χ^2=0.408, OR=0.77 (0.34-1.73)	0.523
Unemployed and ≥ high school	4 (15.4%)	9 (3.8%)	13 (4.9%)	χ^2=3.871, OR=4.22 (1.20-14.74)	0.049
Day Hospital (*vs.* Hospital ward)	19 (73.01%%)	198 (83.5)	217 (82.5%)	χ^2 =1.779, OR=0.53 (0.21-1.36)	0.182
Time since the beginning of care (< 6 months)	18 (75%)	93 (39.2%)	111 (43.3%)	χ^2=8.0639, OR=3.48 (1.45-8.33)	0.003
Solid cancer (*vs.* Hematologic cancer)	25 (96.15%5)	176 (74.26)	201 (76.4%)	χ^2 (Yates)=5.077, OR=8.66 (1.15-65.31)	0.024
SF-12 Tot	30.84±6.32	32.69±6.35	32.15±6.36	F (df 1,261)=1.990	0.159
PHQ9≥7	17 (65.38%)	112 (47.25%)	129 (49%)	χ^2=3.081, OR=2.11 (0.90-4.91)	0.079
TPQ Tot	30.89±5.63	29.51±6.98	29.65±6.85	F (df 1,261)=0.948	0.331
TPQ Serv	14.92±2.86	14.49±3.65	14.53±3.57	F (df 1,261)=0.338	0.562
TPQ Staff	15.88±2.89	15.02±3.55	15.11±3.49	F (df 1,261)=0.1.421	0.234
Cancer Stage 1-2 *vs.* 3-4	0 (0%)	29 (12.2%)	29 (11%)	χ^2=3.576, OR=not calculated	0.059
Palliative (*vs.* other kind of care)	21 (80.8%)	128 (54.0%)	149 (56.6%)	χ^2 6.833, OR=3.58 (1.30-9.80)	0.009

It is well-established that identifying comorbidity with depression can be challenging among people with cancer [16], and it can lead to a substantial decline in their quality of life [5], ultimately having detrimental effects on treatment adherence and outcomes [17-19]. The relatively low relevance of depressive symptoms found in our sample indirectly supports the aforementioned hypothesis.

It is important to emphasize the specific risk associated with individuals who have a high level of education combined with unemployment status. In all such cases, these were relatively young individuals, and it is plausible that an oncological illness occurring at a young age could have a more significant impact on those who have not yet attained professional fulfillment. This may lead to a sense of non-resistance and "letting go" regarding the disease.

The limitations of this study include its cross-sectional nature, the inherently clinical definition of adherence and the utilization of a very simplistic tool to assess it.

Conclusions

The study revealed a low rate of non-adherence to oncological treatments in the examined units. It is hypothesized that the provision of robust psychological and spiritual support to patients may contribute to this favorable adherence rate. Additionally, the study identified a specific risk of non-adherence

among individuals with a high level of education and unemployment. This underscores the significance of giving special consideration to individuals confronted with the demanding task of contending with an oncological disease while experiencing a sense of disillusionment regarding their life aspirations. In this regard, the study highlights the importance of providing focused attention to the psychosocial and spiritual needs of individuals with these characteristics.

Ethics approval:

The research was granted approval by the autonomous Ethics Committee of Azienda Ospedaliero Universitaria di Cagliari, Italy (reference number PG/2018/13269). All processes adhered to the principles of the Helsinki Declaration.

Informed consent:

Each participant provided written informed consent after being furnished with comprehensive explanations of the study's objectives and methods, informed about data security, and guaranteed the option to withdraw their participation at any time.

Availability of data and material:

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interests:

The Authors declare that they have no conflict of interest to disclose.

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Authors Contribution:

FS and MGC: conception and design of the study; OM, CM and EM: acquisition of data, FS and MGC: analysis and interpretation of data; FS: drafting the article; MGC, GLN, GC, FR, GO, MS, AEN: making critical revisions related to the relevant intellectual content of the manuscript; MGC: supervision; all the Authors: validation and final approval of the version of the article to be published.

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