



Original Article

## Epidemiological assessment of distress during chemotherapy: who is affected?



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### المخلص

**أهداف البحث:** بعد ارتفاع معدل الإصابة بالسرطان، ازدادت الحاجة إلى استخدام العلاج الكيميائي وتضاعفت تأثيراته الجانبية أيضا. يعد الضغط النفسي أحد الآثار الجانبية المعروفة، التي لم تلق الاهتمام الكافي. تهدف هذه الدراسة إلى قياس نسبة الضغط النفسي لدى المرضى الخاضعين للعلاج الكيميائي، بخصوص العمر، والجنس، والحالة الاجتماعية وجرعة العلاج الكيميائي، وتقييم رغبة المرضى في مواصلة العلاج الكيميائي.

**طرق البحث:** أجريت دراسة وصفية مستعرضة على مرضى العيادات الخارجية المتلقين لجرعة العلاج الكيميائي التي تتجاوز الجرعة الأولى في مركز النظائر المشعة في الخرطوم. وتم جمع البيانات عبر مقابلة المرضى وجها لوجه وباستخدام مقياس القلق والاكتئاب في المستشفيات.

**النتائج:** كان معدل انتشار القلق والاكتئاب بين المرضى الخاضعين للعلاج الكيميائي ٥٥ (٢٥.٥٪) من بين ٢١٦ مريضا ضمتهم الدراسة، وكانت الأغلبية في منتصف العمر (٣٠-٥٠ عاما) من الإناث المتزوجات. اتبع ظهور الضغط النفسي منحنى على شكل حرف - يو بالإنجليزية بالمقارنة بعدد جرعات العلاج الكيميائي التي تلقوها. وعانى المرضى الذين تلقوا ٥-١ وأكثر من ١٠ جرعات ضغطا نفسيا أكثر من المرضى الذين تلقوا ٦-١٠ جرعات من العلاج الكيميائي. ويرغب أكثر من ٢١٢ (٩٨٪) من المرضى بمواصلة العلاج الكيميائي.

**الاستنتاجات:** في دراستنا، يتقل الضغط النفسي ربع مرضانا المتلقين للعلاج الكيميائي. ويلعب الضغط النفسي دورا في عودة السرطان وشفائه؛ لذلك، يجب أن نعتد منهاجا شاملا لعلاج مرضى السرطان، ويتضمن التقييم النفسي لتحديد المرضى المعرضين للخطر.

**الكلمات المفتاحية:** الضغط النفسي؛ العلاج الكيميائي؛ القلق والاكتئاب؛ السرطان؛ التقييم النفسي

### Abstract

**Objectives:** Following the rise in the incidence of cancer, the need for chemotherapy has escalated, as have its side effects. Psychological distress is one of the known side effects of chemotherapy; however, it has not received adequate attention. The purpose of this study was to measure psychological distress in patients receiving chemotherapy, making comparisons on the basis of age, gender, marital status, and chemotherapy dose, and to assess the patients' willingness to continue with treatment.

**Methodology:** A descriptive cross-sectional study was performed on outpatients receiving chemotherapy beyond the first dose at the Radiation & Isotopes Centre Khartoum (Rick). Data were collected via a face-to-face interview with the patients using the Hospital Anxiety and Depression Scale.

**Results:** Among patients undergoing chemotherapy, 55 (25.5%) experienced anxiety and depression. Of the 216 patients recruited, the majority were middle-aged (30–50 years old) married women. Development of psychological distress followed a U-shaped curve in relation to the number of chemotherapy doses received. Patients who received 1–5 and >10 doses experienced more psychological distress than those who received 6–10 chemotherapy doses. As many as 212 (98%) patients were willing to continue with chemotherapy.

**Conclusion:** In our study, psychological distress burdened a quarter of the patients receiving chemotherapy. Psychological distress plays a role in cancer recurrence and recovery; thus, there is a need for a holistic approach to the management of patients with

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cancer, including psychological evaluation to identify those at risk.

**Keywords:** Anxiety and depression; Cancer; Chemotherapy; Psychological distress; Psychological evaluation

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## Introduction

Recently, the American Cancer Society and National Cancer Institute have reported an increasing cancer incidence, also estimating its further rise.<sup>1</sup> This, in turn, will lead to an increase in the use of chemotherapy since it is considered a cornerstone in treating many types of cancer<sup>2</sup> as well as adjuvant therapy in cancers discovered at advanced stages with poor prognoses, such as pancreatic adenocarcinoma.<sup>3</sup> Chemotherapy varies in duration and regimen, depending on the type and stage of cancer.<sup>4–6</sup>

Although chemotherapy increases cancer survival rates, it has a number of side effects: physiological effects such as fatigue, insomnia, nausea, and vomiting and psychological effects such as fear stemming from uncertainty regarding treatment results and disease recurrence, anxiety, depression, and sadness commonly associated with perceived loss such as losing hair.<sup>7</sup>

Psychological distress is a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional), social, or spiritual nature that may interfere with the patient's ability to cope with the disease.<sup>8</sup> Distress may extend along a continuum from common normal feelings, such as sadness and fear, to disabling conditions, such as depression, anxiety, panic, social isolation, and even existential and spiritual crises.<sup>8</sup> According to *Rieker et al.*, the prevalence of long-term psychological distress ranges from 20% to 66%.<sup>8–10</sup> Anxiety is common in critical periods, such as cancer diagnosis or recurrence, at the beginning of a new treatment, or during illness progression.<sup>8</sup> Depression in patients with cancer, however, can be a normal reaction, a psychiatric disorder, or a somatic consequence of cancer or its treatment.<sup>8</sup>

Among patients with cancer, adverse psychological states have been reported to lead to poorer outcomes and affect cancer recurrence even after treatment. An example of this is presented by *Lazure et al.*, who concluded that depression in patients with head and neck cancer reduces survival, and *Goodwin et al.*, who showed that a recent diagnosis of depression predicted poor survival in patients diagnosed with breast cancer.<sup>11,12</sup>

Considering the above and the fact that the scientific literature does not adequately describe the psychological aspects of patients undergoing chemotherapy, we report here the results of our study on the proportion of psychological distress in patients undergoing chemotherapy and its

association with their age, gender, marital status, and chemotherapy duration.

## Materials and Methods

This was a descriptive, cross-sectional survey performed in March 2010 at the Radiation Isotope Center—Khartoum (RICK), Khartoum state (the only specialised centre of its kind in Sudan).

Sample size calculated using  $n = Z^2Pq \div d^2$  formula

$n$  = sample size

$Z$  = constant value = 1.96

$P$  = prevalence = range of (14–20) the mean = 0.17

$q$  =  $1-p$  =  $1.0-0.17$  = 0.83

$d$  = error allowed = 0.05

$n = 1.96^2 \times 0.17 \times 0.83 \div .05^2 = 216$  patients

A simple random sampling method was used to distribute a questionnaire to a total of 216 male and female patients with cancer, in the age range of 15–65 years, who were receiving chemotherapy. All study participants were out-patients receiving a dose of chemotherapy beyond the first dose.

Data were collected through a face-to-face interview using a pre-structured and pre-tested questionnaire. The questionnaire included demographic and medical information such as age, gender, marital status, diagnosis, and the total number of chemotherapy doses received until recruitment in our study.

Furthermore, the Hospital Anxiety and Depression Scale (HADS), a simple and widely used 14-item questionnaire with two subscales assessing anxiety (HADS-A; seven questions) and depression (HADS-D; seven questions), was completed during the interview. Both the HADS-A and HADS-D have scores ranging from 0 to 21, with higher scores indicating more severe symptoms of anxiety and depression.<sup>13,14</sup> The HADS is not a diagnostic tool; scores are used to measure symptom severity, suggesting the likelihood that a patient may have a disorder. According to *Bjelland et al.*'s review, the HADS is valid for the screening of anxiety and depression in somatic, psychiatric, primary care patients and the general population.<sup>14</sup> This questionnaire was translated into Arabic to facilitate patients' understanding. The Arabic version of the HADS has been validated in previous studies.<sup>30,31</sup> Another tool available to assess patients' psychological state is the Depression, Anxiety and Stress Scales-21, but since our focus was only on anxiety and depression, we decided to choose the more straightforward HADS.<sup>15</sup>

## Statistical analysis

The data were analysed using IBM SPSS Statistics for Windows, version 17 (IBM Corp., Armonk, NY, USA). The association of psychological distress with the patients' age, gender, marital status, and chemotherapy duration was tested using a Chi-square test of significance. The cut-off value for significance was  $p \leq 0.05$ .

**Results**

*Patients' characteristics*

Out of 216 patients, 96 (44.4%) were males and 120 (55.6%) were females, and 159 (73.6%) were married while 57 (26.4%) were unmarried. The age distribution was as follows: there were 38 (17.6%) patients in the age group of 15–30 years, 50 (23.2%) in the age group of 31–46 years, 59 (27.3%) in the age group of 47–52 years, and 69 (31.9%) in the age group of 53–68 years.

The chemotherapy dose distribution was as follows: 117 (54.4%) patients had received a total of 1–5 doses till the time of recruitment, 55 (25.5%) had received 6–10 doses, and 44 (20.3%) patients had received more than 10 doses.

*Patients' psychological state*

Among our participants, 161 (74.5%) did not have anxiety or depression. As per the HADS, the remaining 55 (25.5%) participants had symptoms of psychological distress, namely anxiety (27 participants; 12.5%), depression (10 participants; 4.6%), and both anxiety and depression (18 participants; 8.3%).

*Association of age, gender, marital status, and chemotherapy duration with psychological state (Table 1)*

A total of 47 females versus only eight males were found to be psychologically distressed, and this association was statistically significant ( $p < 0.0001$ ). Regarding age, older patients (31–68 years; 34.3%) were more prone to psychological distress than younger patients (15–30 years; 23.7%) ( $p = 0.2056$ ). Likewise, married patients seemed more prone to psychological distress when undergoing chemotherapy than their unmarried counterparts: 45 versus 10 patients ( $p = 0.1097$ ). Regarding the association of chemotherapy dose and development of psychological distress, 34 patients who had received a

total of 1–5 doses until recruitment were psychologically distressed vs. only eight patients who had received 6–10 doses and this proportion peaked again in patients who had received >10 doses until recruitment. The association of chemotherapy dose with psychological distress was not statistically significant ( $p = 0.0984$ ).

*Types of psychological distress (Table 2)*

Further analyses of the type of psychological distress revealed that 24 (20%) female patients had anxiety, eight (6%) had depression, and 15 (12%) had both anxiety and depression. In males, these figures were three (4%), two (1%), and three (3%), respectively.

Regarding the age distribution of psychological distress, further breakdown of the 31–68 age group showed that anxiety was the main type of psychological distress experienced by patients in this age group.

Psychological distress types in married patients were as follows: 21 (13.2%) had anxiety, eight (5%) had depression, and 16 (10.1%) had both anxiety and depression. Similarly, the most common type of psychological distress among unmarried patients was anxiety (six patients; 10.5%).

Upon categorizing patients by chemotherapy dose, anxiety was still the most common type of psychological distress, affecting 11% of patients who had received 1–5 doses until recruitment, 9% of patients who had received 6–10 doses, and 12.5% of those who had received more than 10 doses until recruitment.

Following the parameters mentioned above, participants were also asked if they intended to continue with chemotherapy and almost all (212; 98.1%) declared their intention to do so, leaving only 4 (1.9%) patients who intended to discontinue.

**Table 1: Association between patient characteristics and development of psychological distress during chemotherapy.**

Variables	Psychological distress (Row%)	No psychological distress (Row%)	<i>p-value</i>
<b>Gender</b>			
Male	8 (8.3%)	88 (91.7%)	$p < 0.0001$ <b>0.0000</b>
Female	47 (39.2%)	73 (60.8%)	
<b>Age group</b>			
15–30	9 (23.7%)	29 (76.3%)	$p = 0.2056$
31–68	61 (34.3%)	117 (65.7%)	
<b>Marital status</b>			
Married	45 (28.3%)	114 (71.7%)	$p = 0.1097$
Unmarried	10 (17.5%)	47 (82.5%)	
<b>Duration of chemotherapy</b>			
1–5 doses	34 (29.1%)	83 (70.9%)	$p = 0.0984$
6–10 doses	8 (14.5%)	47 (85.5%)	
Above 10 doses	13 (29.5%)	31 (70.5%)	

**Table 2: Types of psychological distress.**

Variables	Did not develop anxiety or depression		Developed anxiety		Developed depression		Developed anxiety and depression	
	No.	Row %	No.	Row %	No.	Row %	No.	Row %
<b>Gender</b>								
Male	88	92%	3	4%	2	1%	3	3%
Female	73	62%	24	20%	8	6%	15	12%
<b>Age group</b>								
15–30	29	76%	6	15%	1	2%	2	7%
31–46	30	60%	11	22%	4	8%	5	10%
47–52	38	64%	13	22%	5	8%	3	6%
53–68	49	71%	14	20%	5	7%	1	2%
<b>Marital status</b>								
Married	114	71.1%	21	13.2%	8	5%	16	10.1%
Unmarried	47	82.5%	6	10.5%	2	3.5%	2	3.5%
<b>Duration of chemotherapy</b>								
1–5 doses	83	70.9%	13	11.1%	9	7.7%	12	10%
6–10 doses	47	85.5%	5	9.1%	1	1.8%	2	3.6%
Above 10 doses	31	70.5%	9	12.5%	0	0%	4	9%

## Discussion

Our results revealed that one quarter of patients receiving chemotherapy were psychologically distressed. The majority of these patients were females, older than 30 years, and married. Nevertheless, and despite their psychological distress, almost all patients decided to continue with chemotherapy.

The proportion of psychological distress (25%) reported in our study is relatively low when compared to similar studies focusing on cancer-related psychological changes. A study by *Zainal et al.* reported that the prevalence of depression and anxiety in patients with cancer during chemotherapy was 32%.<sup>8</sup> Such results should not be ignored as many recent studies have reported the relationship between psychological distress and poor outcomes, recurrence, and decreased survival in patients with cancer.<sup>8,11,16–18</sup>

An analysis stratified by gender revealed a high level of psychological distress, specifically anxiety, among our female participants, similar to the results of *Keller et al.*, who reported distress in 54% of their female participants vs. 28% in the male participants.<sup>16</sup> This could be related to a difference in emotional processing between females and males, as well as sex-related cancers such as breast cancer and genital cancer, which are usually related to self-image, disfigurement, and effect on sex drive.<sup>17</sup> Another explanation of this female preponderance, offered by *Bergerot et al.*, is that women use health services more often than men, which, in turn, leads to increased follow-up and registration of women's health data in the health system in comparison to men with the same health/disease conditions.<sup>18</sup>

There is no consensus in the literature about the age cut-off when analysing the frequency of psychological distress in the course of cancer and chemotherapy. Our findings revealed that the proportion of patients younger than 30 years with psychological distress was lower than patients older than 30 years, but this difference was not statistically significant. However, further analysis revealed that psychological distress was slightly more frequent in patients aged 30–50 years than those aged 50–70 years. Similar results were reported by *Bergerot et al.*, who attributed this difference to a higher frequency of encountering practical and physical problems in everyday life among patients aged 40–55 years as compared to those aged 55–70 years.<sup>13</sup>

Recently, *Parker et al.*<sup>19</sup> demonstrated that, in patients with cancer, demographic variables (age, gender, marital status, education) were associated with measures of adjustment and better quality of life (QOL) whereas medical variables (time since diagnosis, recurrence status, treatment variables, stage of disease) were not. Furthermore, patients with more social support reported less anxiety and depression and better QOL in the mental health domain, independent of demographic and medical variables.<sup>19</sup> Contrary to these findings, our results showed a higher frequency of distress and anxiety among married versus unmarried patients. An explanation of this might be that the Arab-African socio-cultural setting of our study involves extended families, where fathers and mothers are burdened with more responsibilities and duties. Although such a family structure might provide social support, it can also prove to be a source of distress if the patient is one of the

main family caregivers. It is essential to assess the level of social support in patients with cancer as this may help identify those at risk for distress.<sup>19</sup>

In the present study, the relationship between psychological distress and the number of chemotherapy doses was as follows: the highest levels of anxiety and depression were recorded at 1–5 doses and (>10 doses), with the lowest level of distress being at the middle point (6–10 doses). The psychological distress experienced at the beginning of chemotherapy is explained in the literature as patients' initial reaction to its side effects before they adapt.<sup>13,20–22</sup> Most patients receiving chemotherapy experience psychological distress as a result of the adverse effects of the chemotherapeutic agents.<sup>23</sup> Nausea and vomiting, tiredness or fatigue, sore mouth, reduced fertility, peripheral neuropathy, and skin problems are common side effects of chemotherapy agents.<sup>8</sup> However, psychological distress experienced at more than 10 doses might represent chronic stress or delayed post-traumatic stress disorder (PTSD).<sup>20,24–26</sup> Individuals with PTSD are typically those who, upon exposure to a traumatic life event, immediately exhibit high levels of psychological distress, after which they appear to recover before relapsing.<sup>20,24</sup>

*Marco et al.* showed that distress and depression led to greater non-compliance among patients with breast cancer who had depression as compared to the controls, where only 51.3% of the former versus 92% of the latter agreed to and received chemotherapy.<sup>26,27</sup>

When we asked whether they would continue with their treatment, almost all our patients declared their intention to continue with chemotherapy. While this is a great outcome from any medical management perspective, this result by itself does not reflect the fact that a quarter of these patients experienced psychological distress. In many institutions worldwide, among patients with cancer, medical management is separated from mental care.<sup>28</sup> Psychological distress in patients undergoing chemotherapy is under-recognised and does not receive adequate attention in medical practice and scientific literature. The integration of mental health and medical services is critical for patients with cancer. A multidisciplinary committee, the office practice, or institution must be responsible for evaluating the quality of the distress management provided using outcome research studies that include QOL assessment and analysis of cost-effectiveness.<sup>28</sup> Such an evaluation would also help increase the medical staff's awareness about the benefits of distress management in patients with cancer. Furthermore, patients and their families should be informed that distress management is part of their total medical care.<sup>28</sup>

### Study limitation

Although we are aware that the type of cancer and its treatment plan, outcome, and prognosis affect psychological distress, in the present study, cancer type<sup>29</sup> was not included as a variable. However, we believe that the inclusion of this information would not have affected the results concerning our main objective, which was to assess psychological distress among (all) patients undergoing chemotherapy.



## Conclusion

In conclusion, one quarter of our patients developed psychological distress, with the majority being females, older than 30 years of age, and married. Some patients might experience distress relief and develop adaptive coping over time. While these patients may not need supportive care interventions, others might be at high risk of developing psychological distress and should be considered for early interventions facilitating adaptive coping processes to address anxiety, depression, and other problems during and following chemotherapy.

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None.

## Conflict of interest

The authors have no conflict of interest to declare.

## Ethical approval

Ethical approval was obtained from the Department of Family and Community Medicine, the University of Khartoum institutional review board. Permission was also obtained from the medical manager of Radiation and Isotope Center Khartoum. Written consent was obtained from all study participants.

## Authors contributions

DYM had a role in choosing the study design and implementing the study; was involved in data collection, analysis, and interpretation; contributed substantially to the writing of this article; and read, edited, and approved its final version. AHI had a role in data analysis and interpretation; contributed substantially to the writing of this article; and read, edited, and approved its final version. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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