Cognitive Dysfunction and Its Predictors in Adult Patients With Cancer Receiving Chemotherapy: A Cross-Sectional Correlational Study

Dhuha Youssef WAZQAR

ABSTRACT

Background: Chemotherapy-related cognitive dysfunction, one of the most frequently reported symptoms in patients with cancer, has a negative impact on the daily lives of patients. No research has examined cognitive dysfunction and its potential predictors in adult patients with cancer receiving chemotherapy in Saudi Arabia.

Purpose: The purpose of this study was to examine the sociodemographic, clinical, and psychological factors associated with cognitive dysfunction in adult patients with cancer receiving chemotherapy.

Methods: A cross-sectional correlational study was carried out with a convenience sample of 100 adult patients with cancer receiving chemotherapy at a university teaching hospital in Saudi Arabia. The Montreal Cognitive Assessment, the Hospital Anxiety and Depression Scale, and sociodemographic and clinical surveys were completed by participants. Descriptive statistics and linear regression were used to analyze the data.

Results: The data showed that the participants experienced moderate-to-severe cognitive dysfunction. Participants performed poorly in the divided attention and memory cognitive domains. Age, educational level, and depression factors were found to be significant predictors of cognitive dysfunction.

Conclusions/Implications for Practice: Cognitive dysfunction is commonly seen in patients with cancer receiving chemotherapy. Chemotherapy, age, and psychological factors increase susceptibility to cognitive dysfunction in adult patients with cancer. Oncology nurses should be aware that patients with cancer may be extremely vulnerable to cognitive dysfunction. Furthermore, age and psychological factors must be considered when developing symptom management and supportive care intervention programs to reduce the incidence of negative cognitive outcomes in this population.

Key Words: patients with cancer, chemotherapy, cognitive dysfunction, oncology nurses.

Introduction

The number of cancer cases worldwide, estimated at 14.1 million in 2012, is on the rise and projected to reach 23.6 million new diagnoses each year by 2030 (World Health Organization, 2018). In Saudi Arabia (SA), 15,653 cancer cases were reported to the Saudi Cancer Registry (SCR) in 2013 (SCR, 2016). Overall, cancer has been more prevalent among Saudi women (8,294, 53%) than Saudi men (7,359, 47%), with a female–male ratio of 120:100 (SCR, 2016). The top three malignancies among Saudi women are breast, thyroid, and colorectal cancers, whereas colorectal cancer, non-Hodgkin's lymphoma, and leukemia are the top three malignancies among Saudi men (SCR, 2016). Improved access to cancer screening, early detection, and effective cancer treatments have increased the cancer survival rate in recent years, with the 5-year age-standardized relative survival reaching as high as 65% in SA (Swaminathan, Lucas, & Sankaranarayanan, 2011). The increasing numbers of patients with cancer and survivors in SA indicate the need for comprehensive assessment and management of the physical and psychological side effects of cancer treatment modalities to ameliorate the impact of these treatments on daily functioning, quality of life, work activities, and community integration both during and after treatment. Research indicates that healthcare providers should identify and manage chemotherapy-related physical symptoms and side effects and provide psychoeducational interventions to reduce the anxiety and depressive symptoms of patients undergoing cancer treatment to improve quality of life (Dai, Yang, Chen, & Tang, 2017; Wu, Chen, Huang, Chang, & Hsu, 2018).

PhD, RN, Assistant Professor, Oncology Nursing and Cancer Care, Faculty of Nursing, Department of Medical Surgical Nursing, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

Copyright © 2019 The Authors. Published by Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Cancer and its treatment modalities such as chemotherapy, radiation therapy, and hormone therapy may cause mental and physical changes, including neurological impairment, that have a negative impact on the capacity of patients to perform daily life activities (Ahles, Root, & Ryan, 2012; Asher & Myers, 2015). Most related studies indicate that 15%–35% of cancer survivors experience cognitive decline months to years after finishing their treatment and about 75% of patients with cancer experience cognitive dysfunction during treatment (Ahles et al., 2012; Janelsins et al., 2011). Chemotherapy is the backbone of treatment for different types of cancer, and although it significantly increases survival, this treatment modality causes various side effects both during and after treatment. Evidence shows, across different healthcare facilities and country settings, that chemotherapy is the most common cancer treatment modality associated with cognitive dysfunction and/or cognitive decline in patients with cancer, although the effects are not universal (Moon, Kim, & Kim, 2011; Oh, 2017; Pendergrass, Targum, & Harrison, 2018). Although potential psychological and physiological mechanisms (e.g., fatigue, depression, microvascular injury, central nervous system toxicity, DNA damage, and inflammation) have been identified (Ahles, 2012), the structural and functional brain changes that underlie the cognitive dysfunctions associated with chemotherapy are not well understood.

Cognitive dysfunction, a major concern among patients with cancer, is usually referred to as “chemo brain” in the lay community (Asher & Myers, 2015). Chemo brain is a common term used in cancer research to refer to the mental cloudiness that patients with cancer report experiencing during and after chemotherapy (Asher & Myers, 2015). Common cognitive changes associated with chemotherapy typically encompass impairments in visuospatial skills, concentration, executive function (e.g., judgment), attention, and memory that may lead to increased stress levels and decreased job performance when higher cognitive abilities are required (Asher & Myers, 2013; Moon et al., 2011). Numerous studies have examined cognitive dysfunction among patients with cancer during and after chemotherapy. One cross-sectional and controlled longitudinal study on patients with breast cancer found a cognitive decline in the areas of verbal fluency in participants receiving chemotherapy as compared with healthy controls at 3-month follow-up assessments (Ahles et al., 2010). Moreover, a longitudinal and prospective study conducted by Bender and his colleagues (2006) found cognitive declines in verbal working and visual memory in patients with breast cancer after chemotherapy treatment. In addition, prior research suggests that cognitive declines in patients with cancer receiving chemotherapy may have a later onset and persist for 20 years after treatment (Koppelmans et al., 2012). Ahles (2012) found that chemotherapy may cause acute cognitive dysfunction as well as delayed effects as the survivor ages, with a variety of factors affecting the slope of change. As most previous studies have examined cognitive decline in patients with breast and colon cancers only, the reasons for cognitive dysfunction in patients with other cancers receiving chemotherapy are largely unknown.

In addition to chemotherapy, other factors such as age, gender, educational level, treatment duration, number of chemotherapy cycles, fatigue, anemia, quality of life, emotional stress, depression, and anxiety have been proposed as related to cognitive dysfunction in patients with cancer. However, the evidence related to these factors is inconsistent (Oh, 2017; Ramalho, 2015; Vearncombe et al., 2009). In a cross-sectional study on adult patients with cancer, Oh (2017) found that cognitive impairment was more obvious in patients who were women, were older, had received cumulative cycles of chemotherapy, and had severe depression and fatigue. Of these factors, age and number of chemotherapy cycles were identified as the strongest predictors, indicating that cognitive function declines with increasing age and numbers of chemotherapy cycles (Oh, 2017). Another cross-sectional study conducted by Von Ah and Tallman (2015) found a significant relationship between anxiety and cognitive dysfunction in a sample of patients with breast cancer receiving chemotherapy ($r = .51, p < .01$). In addition, a study that examined cognitive dysfunction in patients with cancer found that attention decreased in participants who were and were not anxious, visual/executive functions decreased significantly in anxious participants, and memory decreased in participants who were not anxious (Ramalho, 2015). Furthermore, two additional studies assessed the effect of anxiety and depression on memory test performance in different populations (Bender et al., 2008; Yochim, Mueller, & Segal, 2013). On the basis of these findings, anxiety and depression affect certain aspects of memory functioning. Bender et al. (2008) showed a significant positive relationship between depression and cognitive dysfunction after chemotherapy in patients with cancer ($p = .03$). However, some researchers have found that symptomology falling short of the Diagnostic and Statistical Manual of Mental Disorder standards for anxiety and depression, although not related to cognitive dysfunction, may be associated with the perceived cognitive problems frequently described by patients with cancer (Hermelink et al., 2010).

Anemia after chemotherapy treatment has also been associated with cognitive decline, and patients with cancer who become anemic experienced significant decreases in attention and visual memory test performance (Castel et al., 2017). However, only two studies investigated the influence of anemia on cognitive function during and after receiving chemotherapy and found no significant relationship (Oh, 2017; Vearncombe et al., 2009). Vearncombe et al. (2009) found that, although previous studies identified the significance of clinical and psychological variables in patients with cancer, the supporting evidence was contradictory. However, examination of all the related factors has not been extensive, and further investigation is required.

The extent to which chemotherapy and other factors increase the risk of cognitive decline in adult patients with cancer remains unclear, as few studies outside Western nations have investigated cognitive dysfunction and its associated
factors, particularly in patients with breast and colon cancers receiving chemotherapy. Moreover, results vary among studies in terms of the magnitude of cognitive dysfunction, as expressed in the effect sizes. Therefore, a study of adult patients with different types of cancer in a developing country such as SA should help extend the current scholarly understanding and deepen the knowledge of oncology nurses about this phenomenon and promote improvements in the quality of nursing care delivered to adult patients with cancer. This study may also be a beneficial guide for developing symptom management and supportive care interventions for cognitive dysfunction related to chemotherapy in adult patients with cancer. The purpose of this study was to examine the sociodemographic, clinical (chemotherapy cycles/anemia), and psychological (anxiety and depression) factors associated with cognitive dysfunction in adult patients with cancer receiving chemotherapy in SA.

Methods

Design and Sample
This cross-sectional correlational study was designed to identify factors influencing the cognitive functioning in a convenience sample of adult patients with cancer receiving chemotherapy in King Abdulaziz University Hospital (KAUH) in Jeddah City, SA. Green (1991) proposed that the minimum sample size for regression analyses should be 50 with eight additional observations per term. Thus, this study required a sample size of 98 participants for a multiple regression analysis with six independent variables. An initial sample of 112 eligible patients was invited to participate, with 12 later excluded (eight declined to participate and four participants submitted questionnaires with missing data on the main study variables and the Hospital Anxiety and Depression Scale [HADS]). Thus, data from 100 participants were used in the analysis (response rate: 89%). Eligibility criteria included older than 18 years old, diagnosed with cancer at KAUH, had no evidence of a concurrent disease, and currently receiving chemotherapy. Otherwise, eligible patients were excluded if they were older than 65 years old, were on medications that might affect current cognitive function (i.e., anxiolytics, antidepressants, or narcotic analgesics), had a history of psychiatric or neurological disorders, had a history of alcohol or drug abuse, or had evidence of metastatic cancer or relapse. The medical files of all the participants were checked to confirm eligibility and to provide target demographic and clinical data.

Measures

Sociodemographic and clinical characteristics
The sociodemographic data that were collected included age, gender, nationality, marital status, and level of education. Furthermore, data on cancer type and stage, chemotherapy agents used, hemoglobin level, and number of chemotherapy cycles were collected.

Montreal Cognitive Assessment
The one-page Montreal Cognitive Assessment (MoCA) was used to assess the eight cognitive domains of attention (6 points), visuospatial/executive functions (5 points), short-term memory (5 points), naming (3 points), language (3 points), orientation (6 points), and abstraction (2 points). One point was added to the total score for participants with ≤ 12 years of formal education. The MoCA has been translated into several languages and is freely available on the Internet. It covers tasks such as naming, clock drawing, serial subtraction, sentence repetition, and delayed recall task, with a total possible score of 30 points and a score of less than 26 considered abnormal, as defined by the MoCA’s authors (Nasreddine et al., 2005). According to the validation study, the specificity and sensitivity of the MoCA for detecting cognitive decline were 90% and 87%, respectively, compared with 18% and 100%, respectively, for the Mini-Mental Status Examination. The internal consistency of MoCA was also found to be good (Cronbach’s alpha for the standardized items = .83; Nasreddine et al., 2005). The Cronbach’s alpha value for the overall MoCA scale was .79 in this study.

Hospital Anxiety and Depression Scale
The HADS is utilized to assess the risk of depression and anxiety and incorporates 14 items, of which seven measure anxiety (HADS-A) and seven measure depression (HADS-D). There are four possible answers (0–3) for each item, and scores range from 0 to 21 for each subscale. The recommended cutoff point for a diagnosis of anxiety or depression is 8. The HADS questionnaire has been validated using both exploratory and confirmatory factor analyses and item response theory. The reported Cronbach’s alpha ranges from .68 to .93 for HADS-A and from .67 to .90 for HADS-D (Zigmond & Snaith, 1983). In this study, the Cronbach’s alpha for the overall HADS was .82.

Data Collection Procedures
Trained research nurse assistants consecutively invited qualified patients during regular visits to different oncology units in KAUH between January and May 2018. Participants signed written consent forms before enrollment, which included the purpose of research, the usefulness of the study, detailed instructions about completing the questionnaire, and a confidentiality statement. Participants were informed that they were free to withdraw from the study at any time without penalty and that there would be no financial or other gain from their participation. The questionnaires for assessing cognitive function and anxiety and depression risks, including sociodemographic and clinical items, were administered to all of the participants. Assessments of cognitive function by a trained research assistant occurred in each participant’s room using standard instructions. The cognitive function
assessment and self-report questionnaire took approximately 25–30 minutes to complete. The study was approved by KAUH’s Research Ethics Board (Protocol reference no. 509-17).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics Version 24 (IBM, Inc., Armonk, NY, USA). Descriptive statistics were used to characterize the sociodemographic and clinical variables of the participants. The data were screened for linearity, outliers, normality, and collinearity. Multiple linear regression analysis using the enter method was conducted to identify possible predictors of cognitive dysfunction. The MoCA (cognitive domains) was considered as a dependent variable, whereas age, education, chemotherapy cycles, hemoglobin level, anxiety, and depression were treated as independent variables. The level of significance was set at .05 for all analyses. Cronbach’s alpha values were also calculated to estimate the internal consistency of the MoCA and HADS.

Results

Sociodemographic and Clinical Characteristics of the Participants

Most participants were female (78%), mean participant age was 44.0 (SD = 11.7, range: 18–60) years, most of the participants (63%) were non-Saudi nationals, and 75% were married. Less than one third (29%) had not completed high school, 33% had completed high school, and 38% had a college degree. Cancer stage distribution was as follows: Stage I, 17%; Stage II, 40%; and Stage III, 43%. The average number of chemotherapy cycles was 7.0 (SD = 4.9, range: 1–32) cycles, and the mean hemoglobin level was 10.8 (SD = 1.7) g/dl. Participants were receiving one or a combination of chemotherapy agents (5-fluorouracil), paclitaxel (Genexol), oxaliplatin (Elotin), topotecan (Hycamtin), doxorubicin (Adriamycin), cyclophosphamide (Cytoxan, Endoxan), methotrexate (Trexall), hydroxyurea (Hydrea), and vincristine (Oncovin). Participants with a diagnosis of breast cancer accounted for approximately one third of the sample (34%), and the remainder were diagnosed with gastrointestinal cancer (24%), hematological cancers (23%), and other cancers (19%), respectively (Table 1).

Table 2 shows the results of the effect of chemotherapy on the eight domains of the MoCA and HADS scores. The mean MoCA score was 22 (SD = 4.73), with scores ranging from 10 to 29. It should be noted that 56% of participants experienced moderate-to-severe cognitive dysfunction and 24% experienced mild cognitive dysfunction. Participants showed lower scores for the cognitive domains of divided attention and short-term memory. The mean HADS-A score was 5.94 (SD = 3.28), with scores ranging from 0 to 13, and 21% of participants identified as experiencing moderate-to-severe anxiety. The mean HADS-D score was 7.25 (SD = 4.07), with scores ranging from 0 to 19 and 10% of participants experiencing moderate-to-severe depression.

Regression Analyses

Table 3 shows the predictors of cognitive dysfunction based on multiple regression analyses. In the regression model, age (β = -.098), level of education (β = .588), and depression (β = -.160) were the significant predictors of cognitive dysfunction. Of all of the predictors, level of education was the strongest, whereas depression, age, and education together accounted for 42% of the variance in both MoCA and cognitive test scores. The $R^2$ (AR$^2$) of the regression model, including the three significant predictors, was .415 (.396),

TABLE 1. Sociodemographic and Clinical Characteristics of the Participants (N = 100)

| Variable              | M    | Range | SD  |
|-----------------------|------|-------|-----|
| Age (years)           | 44.0 | 18–60 | 11.7|
| Chemotherapy cycle (cycles) | 7.0  | 1–32  | 4.9 |
| Hemoglobin level (g/dl) | 10.8 | 7.4–16.0 | 1.7 |
| Gender                |      |       |     |
| Male                  | 22   | 22    |     |
| Female                | 78   | 78    |     |
| Nationality           |      |       |     |
| Saudi                 | 37   | 37    |     |
| Non-Saudi             | 63   | 63    |     |
| Marital status        |      |       |     |
| Single                | 14   | 14    |     |
| Married               | 75   | 75    |     |
| Divorced              | 9    | 9     |     |
| Widowed               | 2    | 2     |     |
| Education             |      |       |     |
| Primary               | 20   | 20    |     |
| Intermediate          | 9    | 9     |     |
| High school           | 33   | 33    |     |
| At least college      | 38   | 38    |     |
| Cancer stage          |      |       |     |
| I                     | 17   | 17    |     |
| II                    | 40   | 40    |     |
| III                   | 43   | 43    |     |
| Type of cancer        |      |       |     |
| Breast cancer         | 34   | 34    |     |
| Colorectal cancer     | 17   | 17    |     |
| Lymphomas             | 14   | 14    |     |
| Gastric cancer        | 7    | 7     |     |
| Leukemia              | 9    | 9     |     |
| Bone cancer           | 6    | 6     |     |
| Skin cancer           | 5    | 5     |     |
| Lung cancer           | 5    | 5     |     |
| Prostate cancer       | 3    | 3     |     |
As predicted, depression, lower education, and older age were core factors explaining worse cognitive testing.

**Discussion**

The purpose of this study was to explore the impact of socio-demographic, clinical, and psychological factors on the cognitive dysfunction that adult patients with cancer commonly report during chemotherapy. Findings from this study indicated that 56% of the participants had moderate-to-severe cognitive dysfunction, which is consistent with previous studies that found a significantly higher incidence and a severe cognitive decline in patients with cancer who undergo or receive chemotherapy (Lange et al., 2014; Vitali et al., 2017). Moreover, of the various cognitive function domains, only attention (ability to process multiple information or activities simultaneously) and short-term memory were marked by significant decrements in this study. Similarly, prior studies on patients with stomach, breast, and colorectal cancers receiving different chemotherapy agents have identified negative impacts on the attention and memory domains in subgroup analyses (Cruzado et al., 2014; Oh, 2017). Attention is the basis for cognitive function, and decreasing attention negatively affects aspects of daily living such as community integration and work activities (Pendergrass et al., 2018). Physiological evidence supports the theory that chemotherapy affects the integrity of white matter in the brain and reflects cognitive dysfunction (Monje & Dietrich, 2012). Reduced white matter and hippocampal functionality may cause cognitive deficit symptoms in terms of processing speed, memory, and attention (Monje & Dietrich, 2012). However, other studies did not support a relationship between cognitive dysfunction and chemotherapy in patients with cancer but rather reported high rates of depression, anxiety, and

**TABLE 2. Descriptive Statistics for Anxiety, Depression, and Cognitive Function Assessment Scores (N = 100)**

| Variable            | n    | %    | Mean  | SD   | Possible Range | Actual Range |
|---------------------|------|------|-------|------|----------------|--------------|
| MoCA                |      |      | 22.00 | 4.73 | 0–30           | 10–29        |
| ≤ 23                | 56   | 56   |       |      |                |              |
| 24–26               | 24   | 24   |       |      |                |              |
| ≥ 27                | 20   | 20   |       |      |                |              |
| Visuospatial/Executive function | 3.52 | 1.52 | 0–5   |      | 1–5            |              |
| Naming              | 2.71 | 0.49 | 0–3   |      | 1–3            |              |
| Attention           | 3.44 | 1.34 | 0–6   |      | 0–6            |              |
| Language            | 1.73 | 1.01 | 0–3   |      | 0–3            |              |
| Abstraction         | 1.78 | 0.50 | 0–2   |      | 0–2            |              |
| Memory              | 2.36 | 1.64 | 0–5   |      | 0–5            |              |
| Orientation         | 5.53 | 0.86 | 0–6   |      | 2–6            |              |
| HADS                |      |      | 13.19 | 6.13 | 0–42           | 1–31         |
| HADS-A              |      |      | 5.94  | 3.28 | 0–13           | 0–13         |
| 0–7 (normal)        | 55   | 55   |       |      |                |              |
| 8–10 (mid)          | 24   | 24   |       |      |                |              |
| 11–21 (moderate–severe) | 21   | 21   |       |      |                |              |
| HADS-D              |      |      | 7.25  | 4.07 | 0–21           | 0–19         |
| 0–7 (normal)        | 65   | 65   |       |      |                |              |
| 8–10 (mid)          | 25   | 25   |       |      |                |              |
| 11–21 (moderate–severe) | 10   | 10   |       |      |                |              |

Note. MoCA = Montreal Cognitive Assessment; HADS-A = Hospital Anxiety and Depression Scale-Anxiety; HADS-D = Hospital Anxiety and Depression Scale-Depression.

F = 22.660, p < .001. As predicted, depression, lower education, and older age were core factors explaining worse cognitive testing.

**TABLE 3. Significant Predictors of Cognitive Dysfunction in the Participants**

| Variable | B    | SE  | β    | t    | p    |
|----------|------|-----|------|------|-----|
| Age      | −0.039 | .032 | −.098 | −1.235 | .022 |
| Education| 2.467  | .332 | .588  | 7.421 | .000 |
| HADS-D   | −0.231 | .113 | −.160 | −2.049 | .043 |

Note. R² (AR²) = .415 (.396), F(4, 96) = 22.660 (< .001). AR² = adjusted R²; HADS-D = Hospital Anxiety and Depression Scale-Depression.
fatigue (Abu-Helalah, Al-Hanaqa, Alshraideh, Abdulbaqi, & Hijazem, 2014; Moon et al., 2011) that may negatively influence cognitive function. Further research is required to examine the relationships between cognitive dysfunction and psychological factors.

Age, education, and depression were associated with cognitive function in univariate analysis and were identified as significant predictors in multiple regression models, with these three factors explaining 42% of cognitive deterioration. Similarly, a recent study conducted by Oh (2017) on patients with cancer receiving chemotherapy found that age, gender, and depression had significant, discrete effects on cognitive decline and that these variables together explained 49.6% of the cognitive decline. However, these findings are in contrast to Moon et al. (2011), who suggested that although age and educational level were related to cognitive function in a univariate analysis, they were not significant predictors in multiple regression models. Future research may consider whether age and educational level moderate the effects of depression on cognitive function. Given that 49% of the participants in this study were adults older than 50 years old, the observed cognitive dysfunction may relate to the effects of aging. With increasing research into the cognitive changes in adult patients with cancer receiving chemotherapy, the influence of chemotherapy on the prevalence of dementia in older adult patients has become a significant focus of concern (Lange et al., 2014). Therefore, this issue must be considered when developing intervention programs to enhance cognitive function in this population.

Previous research has examined the correlations between cognitive dysfunction and depression and anxiety. This study found that depression contributed to cognitive dysfunction ($\beta = .21$), which is consistent with the findings of three previous studies conducted on patients with cancer (Bender et al., 2006; Moon et al., 2011; Oh, 2017), although the effect in this study was small and weaker than the effect of either age or educational level. The nonsignificant relationship between anxiety and cognitive decline that was found in this study suggests that cognitive dysfunction in patients with cancer is more closely associated with sociodemographic and clinical variables than with psychological variables. Kaiser, Bledowski, and Dietrich (2014) suggest that cognitive decline in some patients with cancer may be more indicative of emotional suffering than actual cognitive deficits. In this study, 35% of the participants showed signs of depression and 45% showed signs of anxiety, suggesting that screening for mental health conditions such as anxiety and depression may be important because these conditions are common in patients with cancer and because their underlying mechanisms are difficult to identify (Oh, 2017).

It has been reported that low hemoglobin level (anemia) and number of chemotherapy cycles are contributors of cognitive dysfunction in patients with cancer (Castel et al., 2017; Oh, 2017). Vearncombe et al. (2009) stated that hemoglobin was found to be independent of self-report measures and may provide a useful clinical indicator for risk of cognitive dysfunction. Furthermore, Oh (2017) noted that greater cognitive decline occurred in patients with cancer receiving chemotherapy in high doses over long periods. However, this study found no significant effect for either chemotherapy cycles or anemia.

**Limitations**

This study is affected by several limitations. The convenience sample of 100 adult patients with cancer in one geographic location (Jeddah, SA) reduces the generalizability of the findings. However, this study provides insights for decision makers and oncology nurses regarding the importance of developing symptom management and supportive care intervention programs targeting chemotherapy-related cognitive dysfunction for patients with cancer to improve quality of life in this vulnerable population. A second limitation of this study was the use of a cross-sectional design only at one point in time and without a control group. The impact of psychological factors on cognitive function during and after chemotherapy must be examined longitudinally. A third limitation was the lack of current studies in the field of oncology nursing on this topic in SA to allow for a direct comparison of findings. Thus, the direct comparison of results with existing studies was limited. A replication of this study on a large sample of older and middle-aged adult and pediatric patients with cancer being treated in public and private cancer care settings at different geographic locations in SA will be required to compare and contrast specific findings. Finally, study findings were obtained from adult patients with various cancers undergoing treatment with various chemotherapy agents. Thus, it remains unclear whether the observed cognitive dysfunction may be associated with certain cancers or chemotherapy agents or even other treatment modalities.

**Conclusions**

Cognitive dysfunction is commonly seen in adult patients with cancer. More of the participants receiving chemotherapy exhibited a moderate-to-severe decline in cognitive function, with some affected by significant levels of anxiety and depression. Notably, most of the participants in this study were affected by reduced attention and memory loss, which may significantly affect many aspects of life. The results of this study support previous research on cognitive dysfunction in patients with cancer receiving chemotherapy. Age, educational level, and depression were shown to be significant predictive factors for cognitive dysfunction in patients with cancer, explaining 42% of the variance. Further research in this area is necessary. In clinical settings, patients with cancer should be screened for cognitive dysfunction and oncology nurses should consider the effect of mood changes on cognitive function. A multidisciplinary approach involving assessment, education, monitoring, and rehabilitation will be necessary to improve the cognitive functioning of this population in SA.
Acknowledgments

The author would like to thank Barehen Nahouli, Enas Noorwall, Dena Baker, Razan Bugis, and Myan Abukhashba for their help in collecting data from the study participants. Special thanks go out to Ms. Kholood Mansouri, a statistical analyst who helped the author conduct the statistical analysis and interpretation.

Accepted for publication: February 13, 2019
Address correspondence to: Dhuha Youssef WAZQAR, P.O. Box 42828, Jeddah 21551, Kingdom of Saudi Arabia. Tel: +966 544555902; E-mail: dwaqzer@kau.edu.sa
The author declares no conflicts of interest.

Cite this article as:
Wazqar, D. (2019). Cognitive dysfunction and its predictors in adult patients with cancer receiving chemotherapy: A cross-sectional correlational study. The Journal of Nursing Research, 27(6), e56. https://doi.org/10.1097/jnr.0000000000000340

References

Abu-Helalah, M., Al-Hanaqta, M., Alshraideh, H., Abdulbaqi, N., & Hijazeen, J. (2014). Quality of life and psychological well-being of breast cancer survivors in Jordan. Asian Pacific Journal of Cancer Prevention, 15(14), 5927–5936. https://doi.org/10.7314/APJCP.2014.15.14.5927

Ahles, T. A. (2012). Brain vulnerability to chemotherapy toxicities. Psycho-Oncology, 21(11), 1141–1148. https://doi.org/10.1002/pon.3196

Ahles, T. A., Root, J. C., & Ryan, E. L. (2012). Cancer- and cancer treatment-associated cognitive change: An update on the state of the science. Journal of Clinical Oncology, 30(30), 3675–3686. https://doi.org/10.1200/JCO.2012.43.0116

Ahles, T. A., Saykin, A. J., McDonald, B. C., Li, Y., Furstenberg, C. T., Hanscom, B. S., … Kaufman, P. A. (2010). Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: Impact of age and cognitive reserve. Journal of Clinical Oncology, 28(29), 4434–4440. https://doi.org/10.1200/JCO.2009.27.0827

Asher, A., & Myers, J. S. (2015). The effect of cancer treatment on cognitive function. Clinical Advances in Hematology and Oncology, 13(7), 441–450.

Bender, C. M., Pacella, M. L., Sereika, S. M., Brufsky, A. M., Vogel, V. G., Rastogi, P., … Ryan, C. M. (2008). What do perceived cognitive problems reflect? The Journal of Supportive Oncology, 6(5), 238–242.

Bender, C. M., Sereika, S. M., Berga, S. L., Vogel, V. G., Brufsky, A. M., Paraska, K. K., & Ryan, C. M. (2006). Cognitive impairment associated with adjuvant therapy in breast cancer. Psycho-Oncology, 15(5), 422–430. https://doi.org/10.1002/pon.964

Castel, H., Denouel, A., Lange, M., Tonon, M. C., Dubois, M., & Joly, F. (2017). Biomarkers associated with cognitive impairment in treated cancer patients: Potential predisposition and risk factors. Frontiers in Pharmacology, 8, 138. https://doi.org/10.3389/fphar.2017.00138

Cruzado, J. A., Lopez-Santiago, S., Martinez-Marin, V., Jose-Moreno, G., Custodio, A. B., & Feliu, J. (2014). Longitudinal study of cognitive dysfunctions induced by adjuvant chemotherapy in colon cancer patients. Support Care in Cancer, 22(7), 1815–1823. https://doi.org/10.1007/s00520-014-2147-x

Dai, Y. L., Yang, C. T., Chen, K. H., & Tang, S. T. (2017). Changes in and determinants of quality of life in patients with advanced non-small-cell lung cancer undergoing initial chemotherapy. The Journal of Nursing Research, 25(3), 203–215. https://doi.org/10.1097/jnr.0000000000000148

Green, S. B. (1991). How many subjects does it take to do a regression analysis. Multivariate Behavioral Research, 26(3), 499–510. https://doi.org/10.1207/s15327906mb2603_7

Hermelink, K., Küchenhoff, H., Untch, M., Bauerfeind, I., Lux, M. P., Bühner, M., … Münzel, K. (2010). Two different sides of ‘chemobrain’: Determinants and nondeterminants of self-perceived cognitive dysfunction in a prospective, randomized, multicenter study. Psycho-Oncology, 19(12), 1321–1328. https://doi.org/10.1002/pon.1695

Janelins, M. C., Kohli, S., Mohile, S. G., Usuki, K., Ahles, T. A., & Morrow, G. R. (2011). An update on cancer- and chemotherapy-related cognitive dysfunction: Current status. Seminars in Oncology, 38(3), 431–438. https://doi.org/10.1053/j.seminoncol.2011.03.014

Kaiser, J., Bledowski, C., & Dietrich, J. (2014). Neural correlates of chemotherapy-related cognitive impairment. Cortex, 54, 33–50. https://doi.org/10.1016/j.cortex.2014.01.010

Koppelmans, V., Breterel, M. M., Boogerd, W., Seynaeve, C., Gundy, C., & Schagen, S. B. (2012). Neuropsychological performance in survivors of breast cancer more than 20 years after adjuvant chemotherapy. Journal of Clinical Oncology, 30(10), 1080–1086. https://doi.org/10.1200/JCO.2011.37.0189

Lange, M., Rigal, O., Clarisse, B., Giffard, B., Sevin, E., Barillet, M., … Joly, F. (2014). Cognitive dysfunctions in elderly cancer patients: A new challenge for oncologists. Cancer Treatment Reviews, 40(6), 810–817. https://doi.org/10.1016/j.ctrv.2014.03.003

Monje, M., & Dietrich, J. (2012). Cognitive side effects of cancer therapy demonstrate a functional role for adult neurogenesis. Behavioral Brain Research, 227(2), 376–379. https://doi.org/10.1016/j.bbr.2011.05.012

Moon, S., Kim, S. H., & Kim, M. J. (2011). Perceived cognitive function and related factors in Korean women with breast cancer. Asian Nursing Research, 5(2), 141–150. https://doi.org/10.1016/S1976-1317(11)60022-4

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., … Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society, 53(4), 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x

Oh, P. J. (2017). Predictors of cognitive decline in people with cancer undergoing chemotherapy. European Journal of Oncology Nursing, 27, 53–59. https://doi.org/10.1016/j.ejon.2016.12.007

Pendergrass, J. C., Targum, S. D., & Harrison, J. E. (2018). Cognitive impairment associated with cancer: A brief review. Innovation in Clinical Neuroscience, 15(1-2), 36–44.

Ramalho, M. P. M. (2015). Cognitive decline among breast cancer patients. (Unpublished doctoral dissertation). Retrieved from https://pdfs.semanticscholar.org/06ee/147b53eadd9e1388da19b3099cc22d92113.pdf

Saudi Cancer Registry. (2016). Cancer incidence report Saudi Arabia. Retrieved from https://nhic.gov.sa/eServices/Documents/2013.pdf
Swaminathan, R., Lucas, E., & Sankaranarayanan, R. (2011). Cancer survival in Africa, Asia, the Caribbean and Central America: Database and attributes. *IARC Scientific Publications, 162*, 23–31.

Vearncombe, K. J., Rolfe, M., Wright, M., Pachana, N. A., Andrew, B., & Beadle, G. (2009). Predictors of cognitive decline after chemotherapy in breast cancer patients. *Journal of the International Neuropsychological Society, 15*(6), 951–962. https://doi.org/10.1017/S1355617709990567

Vitali, M., Ripamonti, C. I., Roila, F., Proto, C., Signorelli, D., Imbimbo, M., … Lo Russo, G. (2017). Cognitive impairment and chemotherapy: A brief overview. *Critical Reviews in Oncology/Hematology, 118*, 7–14. https://doi.org/10.1016/j.critrevonc.2017.08.001

Von Ah, D., & Tallman, E. F. (2015). Perceived cognitive function in breast cancer survivors: Evaluating relationships with objective cognitive performance and other symptoms using the functional assessment of cancer therapy-cognitive function instrument. *Journal of Pain and Symptom Management, 49*(4), 697–706. https://doi.org/10.1016/j.jpainsymman.2014.08.012

World Health Organization. (2018). *Worldwide cancer statistics*. Retrieved from http://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwide-cancer

Wu, P. H., Chen, S. W., Huang, W. T., Chang, S. C., & Hsu, M. C. (2018). Effects of a psychoeducational intervention in patients with breast cancer undergoing chemotherapy. *The Journal of Nursing Research, 26*(4), 266–279. https://doi.org/10.1097/jnr.0000000000000252

Yochim, B. P., Mueller, A. E., & Segal, D. L. (2013). Late life anxiety is associated with decreased memory and executive functioning in community dwelling older adults. *Journal of Anxiety Disorders, 27*(6), 567–575. https://doi.org/10.1016/j.janxdis.2012.10.010

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*(6), 361–370.