

Original Research Article

Assessment of chemotherapy-induced cognitive impairment in cancer patients

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Received: 12 August 2026

Accepted: 18 September 2026

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ABSTRACT

Background: Chemotherapy-induced cognitive impairment (CICI) is a well-established side-effect of cancer treatment, which can impact memory, attention, executive function and quality of life. There have been reports of cognitive impairment in chemotherapy-treated patients, but there is limited data in the Indian population. This study was conducted to assess the prevalence of CICI and identify factors associated with cognitive impairment among patients undergoing chemotherapy.

Methods: A cross-sectional observational study was performed among 160 adult cancer patients receiving chemotherapy treatment at a tertiary care center. The functional assessment of cancer therapy – cognitive function (FACT-Cog, version 3) questionnaire was used to measure cognitive function. A structured case record form was used to gather the demographic and clinical information. Descriptive statistics, correlation analysis and multivariable logistic regression were used for statistical analysis to find independent predictors of cognitive impairment.

Results: Among 160 participants, 57 (35.6%) had chemotherapy induced cognitive impairment. Cognitive function was significantly associated with advanced cancer stage and number of chemotherapy cycles and was an independent predictor of cognitive impairment in multivariable analyses. Type 2 diabetes mellitus was associated with lower odds of cognitive impairment, although this finding requires further investigation.

Conclusions: Cognitive impairment was common among patients who were receiving chemotherapy. Greater treatment exposure and advanced disease stage were independently associated with cognitive impairment, highlighting the importance of routine cognitive assessment during cancer treatment. Further prospective multicenter studies are needed to confirm these findings and improve the management of chemotherapy-induced cognitive impairment.

Keywords: Chemotherapy-induced cognitive impairment, Cancer, FACT-Cog, Cognitive function, Chemotherapy

INTRODUCTION

Cancer is a major public health challenge and remains one of the leading causes of illness and death worldwide. Advances in cancer diagnosis and treatment have improved survival rates considerably, allowing many patients to live longer after treatment. As survival has improved, increasing attention has shifted toward treatment-related adverse effects that can affect patients' quality of life.¹ One such complication is chemotherapy-induced cognitive impairment (CICI), commonly known

as "chemobrain," which has gained recognition as an important issue in cancer survivorship.

Chemotherapy-induced cognitive impairment refers to a decline in cognitive functions such as memory, attention, concentration, executive function, and information processing speed that develops during or after cancer treatment. The underlying mechanisms are complex and are likely influenced by both treatment-related and patient-related factors. Proposed mechanisms include systemic inflammation, oxidative stress, hormonal alterations,

fatigue, anxiety, depression, sleep disturbances, and the effects of other cancer therapies.^{2,3}

The prevalence of chemotherapy-induced cognitive impairment varies considerably depending on the cancer type, treatment regimen, assessment method, and timing of evaluation. Approximately 25–75% of patients experience cognitive impairment during or after chemotherapy, while objective neuropsychological assessments identify cognitive deficits in nearly one-third of patients following treatment.⁴ Although cognitive function improves in many patients after completion of therapy, a substantial proportion continue to experience persistent cognitive difficulties for months or even years, adversely affecting their daily functioning and quality of life.⁵

Assessment of cognitive impairment has increasingly incorporated patient-reported outcome measures in addition to objective neuropsychological tests. The functional assessment of cancer therapy–cognitive function (FACT-Cog) questionnaire is one of the most widely accepted instruments for evaluating perceived cognitive impairment in patients with cancer. It assesses multiple domains, including perceived cognitive impairment, perceived cognitive abilities, comments from others, and the impact of cognitive changes on quality of life. Owing to its reliability, validity, and ease of administration, the FACT-Cog has been widely used in both clinical practice and research.⁶

Despite growing awareness of chemotherapy-induced cognitive impairment worldwide, evidence from India remains limited. Most available studies have focused on individual cancer types or relatively small patient populations, limiting the generalizability of their findings. Furthermore, data on the demographic and clinical factors associated with cognitive impairment among patients receiving chemotherapy remain limited, particularly in routine oncology practice.^{7,8} Understanding the burden of cognitive impairment and the factors associated with its occurrence may facilitate early recognition and appropriate supportive interventions.

Therefore, the present study aimed to assess cognitive impairment among cancer patients undergoing chemotherapy and to identify factors associated with its occurrence during chemotherapy treatment.

METHODS

Study design and setting

A hospital-based cross-sectional observational study was conducted over a period of six months from April 2025 to September 2025 in the Department of Oncology, Employees' State Insurance Corporation Medical College and Post Graduate Institute of Medical Sciences and Research (ESIC-MC and PGIMSR), Rajajinagar, Bengaluru. The study included cancer patients receiving chemotherapy who attended the oncology outpatient department.

Study participants

Adult patients aged 18–70 years with a confirmed diagnosis of any malignancy who had completed at least three cycles of chemotherapy were considered eligible for the study. Patients who provided written informed consent were included. Patients with known psychiatric illness (schizophrenia and major depressive disorder) that might affect cognitive function, history of stroke, traumatic brain injury, epilepsy, or multiple sclerosis, and patients receiving medications that could impair cognition, such as benzodiazepines, anticholinergics, opioids or antidepressant drugs, were not included.

Sample size

The sample size was determined using the standard formula for estimating a single proportion assuming a prevalence of 4%, a 95% confidence level, and a precision of 5%. The minimum sample size calculated was 159. The study included 160 participants who satisfied the eligibility criteria.

Data collection

Following approval from the Institutional Ethics Committee, patients who fulfilled the eligibility criteria were invited to participate in the study. Written informed consent was obtained from all participants before data collection. Information on age, sex, cancer type, duration of illness, chemotherapy cycles completed, and associated comorbidities was collected using a case record form developed for the study.

FACT-Cog version 3, a validated patient-reported questionnaire was used to determine cognitive function among cancer patients. This patient-reported questionnaire measures four domains of cognitive function: perceived cognitive impairment (PCI), perceived cognitive abilities (PCA), comments from others (Cog-O), and the impact of cognitive changes on quality of life (Cog-QoL). Participants with a CogPCI score below 54 were considered to have cognitive impairment.

Outcome measures

Assessment of cognitive impairment among patients undergoing chemotherapy was the primary outcome while the secondary outcome was the identification of demographic and clinical factors associated with cognitive impairment.

Statistical analysis

Data was entered into Microsoft Excel and analysed using IBM statistical package for the social sciences (SPSS) statistics version 29. Mean±standard deviation (SD) or median with interquartile range (IQR) were used to express continuous variables, while frequencies and percentages were used for categorical variables.

Independent t-test or Mann–Whitney U test were used for comparisons between two groups, while one-way ANOVA or Kruskal–Wallis test was used for >2 groups. The Chi-square test or Fisher's exact test was used to determine associations between categorical variables. Multivariate logistic regression analysis was used to determine factors associated with cognitive impairment. Statistical significance was considered at $p < 0.05$.

Ethical considerations

Ethical approval to conduct the study was obtained from ESIC-MC and PGIMSR, Rajajinagar, Bengaluru. All participants provided written informed consent prior to enrollment and confidentiality of patient information was ensured throughout the study.

RESULTS

The study included 160 patients undergoing chemotherapy. Most participants were between 41 and 60 years of age (60.6%), followed by those older than 60 years (23.1%). Only 1.8% of the study population belonged to the 18–25-year age group. Females accounted for 63.1% of the participants. Nearly half of the participants had a normal body mass index (49.3%), whereas 36.2% were overweight. Most patients had completed 1–5 (44.3%) or 6–10 (43.8%) cycles of chemotherapy. Regarding comorbidities, 38.1% of patients had three or more comorbid conditions, while 16.9% had no comorbidities. Hypertension (66.9%) and type 2 diabetes mellitus (51.9%) were the most frequently reported comorbid conditions, followed by hypothyroidism (23.1%), ischemic heart disease (21.3%), and chronic kidney disease (20.0%) (Table 1).

Among the 160 study participants, 57 (35.6%) were identified as having chemotherapy-induced cognitive impairment based on the FACT-Cog Perceived Cognitive Impairment (CogPCI) subscale, while 103 (64.4%) showed no evidence of cognitive impairment. The mean FACT-Cog domain scores were 54.84 ± 13.40 for CogPCI, 20.69 ± 5.40 for CogPCA, 12.99 ± 3.06 for CogOth, and 12.31 ± 3.09 for CogQOL (Table 2 and Figure 1).

The prevalence of cognitive impairment varied across demographic, clinical, disease, and treatment characteristics. Cognitive impairment was more common among females (39.6%) than males (28.8%). The proportion of patients with cognitive impairment increased progressively with the number of chemotherapy cycles completed, from 8.4% among those who had received 1–5 cycles to 100.0% among those who had completed more than 15 cycles. Patients with three or more comorbidities (44.1%) and those with ischemic heart disease (44.1%) showed a higher prevalence of cognitive impairment than other comorbidity groups. Among the different cancer types, the highest prevalence was observed in patients with hematological/lymphatic malignancies (47.3%), followed by respiratory (43.7%) and breast cancers (37.9%). Among

chemotherapy drug classes, cognitive impairment was most frequently observed in patients receiving monoclonal antibodies (35.6%) and platinum-based chemotherapy (34.7%) (Table 3).

Table 1: Baseline demographic and clinical characteristics of the study participants.

Characteristics	Frequency (N)	Percentage (%)
Age (years)		
18–25	3	1.8
26–40	23	14.3
41–60	97	60.6
>60	37	23.1
Gender		
Male	59	36.9
Female	101	63.1
Body mass index (kg/m²)		
Underweight (<18.5)	8	5
Normal (18.5–24.9)	79	49.3
Overweight (25.0–29.9)	58	36.2
Obese class I (30.0–34.9)	7	4.3
Obese class II (35.0–39.9)	7	4.3
Obese class III (≥ 40)	1	0.6
Chemotherapy cycles completed		
1–5	71	44.3
6–10	70	43.8
11–15	15	9.4
16–20	4	2.5
Number of comorbidities		
None	27	16.9
One	31	19.4
Two	41	25.6
Three or more	61	38.1
Comorbid conditions		
Hypertension	107	66.9
Type 2 diabetes mellitus	83	51.9
Hypothyroidism	37	23.1
Ischemic heart disease	34	21.3
Chronic kidney disease	32	20

*Percentages for comorbid conditions do not total 100% because individual patients could have more than one comorbidity

Table 2: Prevalence of cognitive impairment and FACT-Cog domain scores among study participants.

Variables	Category/domain	Value
Cognitive impairment status	Yes	57 (35.6%)
	No	103 (64.4%)
FACT-Cog domain scores	CogPCI (mean $\pm$ SD)	54.84 ± 13.40
	CogPCA (mean $\pm$ SD)	20.69 ± 5.40
	CogOth (mean $\pm$ SD)	12.99 ± 3.06
	CogQOL (mean $\pm$ SD)	12.31 ± 3.09

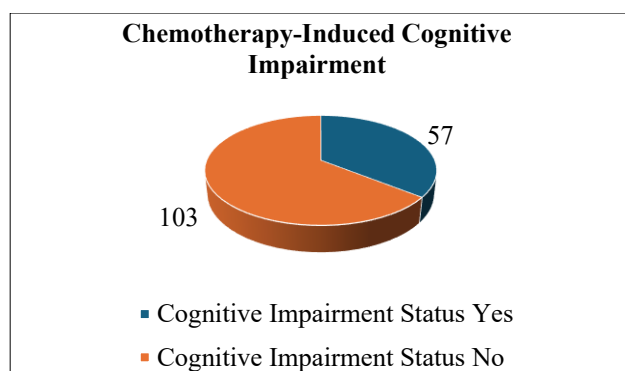


Figure 1: Prevalence of chemotherapy-induced cognitive impairment among cancer patients.

The association between demographic and clinical characteristics and FACT-Cog domain scores was evaluated using appropriate statistical tests. Among the variables assessed, ischemic heart disease showed a significant association with all four FACT-Cog domains, including CogPCI ($p=0.019$), CogPCA ($p=0.022$), CogOth ($p=0.016$), and CogQOL ($p=0.013$). No significant associations were observed between FACT-Cog domain scores and cancer type, gender, hypertension, type 2 diabetes mellitus, hypothyroidism, or chronic kidney disease (Table 4).

Chemotherapy cycles completed showed a significant negative correlation with all FACT-Cog domain scores, including CogPCI ($r=-0.512$, $p<0.001$), CogPCA ($r=-0.487$, $p<0.001$), CogOth ($r=-0.516$, $p<0.001$), and CogQOL ($r=-0.523$, $p<0.001$), indicating poorer cognitive function with increasing chemotherapy exposure. Cancer stage was also significantly associated with all FACT-Cog domains ($p<0.001$). In contrast, age and body mass index were not significantly correlated with any of the FACT-Cog domain scores (Table 5).

Multivariable logistic regression analysis identified stage of cancer and the number of chemotherapy cycles completed as independent predictors of cognitive impairment. Advanced cancer stage was associated with a more than threefold increase in the odds of cognitive impairment (OR=3.151, 95% CI: 1.768–5.617; $p=0.0001$), while each increase in chemotherapy exposure was associated with higher odds of cognitive impairment (OR=2.438, 95% CI: 1.810–3.283; $p<0.001$). Type 2 diabetes mellitus was independently associated with lower odds of cognitive impairment (OR=0.422, 95% CI: 0.204–0.874; $p=0.020$). Age, gender, body mass index, hypertension, ischemic heart disease, hypothyroidism, and chronic kidney disease were not significantly associated with cognitive impairment after adjustment for other variables (Table 6).

Table 3: Prevalence of cognitive impairment according to demographic, clinical, disease, and treatment characteristics.

Characteristics	Category	Total patients (N)	Patients with cognitive impairment, N (%)
Age (years)	18–25	3	1 (33.3)
	26–40	23	8 (34.7)
	41–60	97	34 (35.1)
	>60	37	14 (37.8)
Gender	Female	101	40 (39.6)
	Male	59	17 (28.8)
Chemotherapy cycles	1–5	71	6 (8.4)
	6–10	70	33 (47.1)
	11–15	15	14 (93.3)
	>15	4	4 (100.0)
Number of comorbidities	None	27	17 (40.6)
	One	31	22 (30.1)
	Two	41	8 (37.8)
	≥ 3	61	10 (44.1)
Type of comorbidity	Hypertension	107	40 (37.3)
	Type 2 diabetes mellitus	83	25 (30.1)
	Ischemic heart disease	34	15 (44.1)
	Hypothyroidism	37	14 (37.8)
	Chronic kidney disease	32	13 (40.6)
Cancer type	Breast	58	22 (37.9)
	Gastrointestinal	28	9 (32.1)
	Hematological/lymphatic	19	9 (47.3)
	Respiratory	16	7 (43.7)
	Gynecological	16	5 (31.2)
	Genitourinary	9	3 (33.3)

Continued.

Characteristics	Category	Total patients (N)	Patients with cognitive impairment, N (%)
Chemotherapy drug class	Head and neck	9	2 (22.2)
	Miscellaneous	5	1 (20.0)
	Platinum-based	75	26 (34.7)
	Taxanes	45	13 (28.9)
	Monoclonal antibodies	73	26 (35.6)
	Vinca alkaloids	7	1 (14.3)
	Anthracyclines	30	8 (26.7)
	Topoisomerase I inhibitor	6	1 (16.7)
	Antimetabolites	25	4 (16.0)
	Other agents	4	1 (25.0)

Table 4: Association of demographic and clinical characteristics with FACT-Cog domain scores.

Characteristics	Statistic	Cog PCI p value	Cog PCA p value	Cog Oth p value	Cog QOL p value
Cancer type	χ^2	0.952	0.919	0.587	0.997
Gender	U	0.631	0.535	0.512	0.461
Hypertension	U	0.262	0.577	0.606	0.356
Type 2 diabetes mellitus	U	0.458	0.36	0.361	0.082
Ischemic heart disease	U	0.019	0.022	0.016	0.013
Hypothyroidism	U	0.085	0.963	0.203	0.312
Chronic kidney disease	U	0.222	0.753	0.186	0.174

Table 5: Correlation of chemotherapy cycles, age, body mass index, and cancer stage with FACT-Cog domain scores.

Variables	Statistic	Cog PCI	Cog PCA	Cog Oth	Cog QOL
Chemotherapy cycles completed	r	-0.512	-0.487	-0.516	-0.523
	P value	<0.001	<0.001	<0.001	<0.001
Age (years)	r	-0.128	-0.110	-0.029	-0.035
	P value	0.107	0.166	0.718	0.662
Body mass index (kg/m ²)	r	-0.117	-0.058	-0.067	-0.100
	P value	0.142	0.469	0.397	0.208
Cancer stage	χ^2	25.3	13.1	19.1	14.5
	P value	<0.001	<0.001	<0.001	<0.001

Table 6: Multivariable logistic regression analysis of factors associated with cognitive impairment.

Variables	Regression coefficient (β)	Std. error	Odds ratio (95% CI)	P value
Age (years)	0.003	0.015	1.003 (0.975–1.033)	0.822
Female gender	0.335	0.358	1.398 (0.694–2.818)	0.349
Body mass index (kg/m ²)	0.012	0.038	1.012 (0.939–1.091)	0.752
Hypertension	0.487	0.393	1.627 (0.754–3.513)	0.215
Type 2 diabetes mellitus	-0.862	0.371	0.422 (0.204–0.874)	0.020
Ischemic heart disease	0.522	0.412	1.686 (0.752–3.782)	0.205
Hypothyroidism	-0.015	0.429	0.985 (0.425–2.282)	0.972
Chronic kidney disease	0.343	0.448	1.409 (0.586–3.389)	0.444
Stage of cancer	1.148	0.295	3.151 (1.768–5.617)	0.0001
Number of chemotherapy cycles completed	0.89	0.152	2.438 (1.810–3.283)	<0.001

DISCUSSION

The present study included 160 patients receiving chemotherapy for different malignancies, with most

participants belonging to the 41–60 years' age group. Female patients constituted a larger proportion of the study population, which is likely due to the higher number of breast cancer cases included in the study. The majority of

patients had completed between one and ten chemotherapy cycles and had one or more coexisting medical conditions, with hypertension and type 2 diabetes mellitus being the most frequently reported comorbidities. These findings reflect the typical clinical profile of patients attending oncology services and provide a representative population for evaluating chemotherapy-induced cognitive impairment. Similar patient characteristics have been reported by Janelins et al whose multicentre longitudinal study predominantly included women with breast cancer receiving chemotherapy, and by Brezden et al who also evaluated cognitive function among patients undergoing adjuvant chemotherapy for breast cancer.^{9,10} Although the distribution of cancer types varies across studies, they collectively demonstrate that cognitive impairment is a clinically relevant concern in patients receiving systemic chemotherapy irrespective of the underlying malignancy.

In the present study, 35.6% of patients experienced chemotherapy-induced cognitive impairment based on the FACT-CogPCI subscale. This finding is comparable with the existing literature, which suggests that cognitive impairment is a common adverse effect of chemotherapy. Whittaker et al in a systematic review and meta-analysis of 52 studies, reported that approximately one in three breast cancer survivors experienced clinically significant cognitive impairment.¹¹ The authors also found that the prevalence was 44% when assessed using self-reported measures and 21–34% when objective neuropsychological tests were used. Furthermore, the present study assessed cognitive impairment using the validated FACT-Cog instrument and the recommended PCI cut-off, which has been shown by Van Dyk et al to reliably identify patients with clinically meaningful cognitive impairment, thereby supporting the validity of our findings.⁶

In the present study, ischemic heart disease was significantly associated with poorer scores across all FACT-Cog domains, suggesting worse patient-reported cognitive function among affected patients. Although direct evidence linking ischemic heart disease with chemotherapy-related cognitive impairment is limited, Maurer et al highlighted that vascular dysfunction is an important contributor to cognitive impairment.¹² They described mechanisms such as endothelial dysfunction, reduced cerebral perfusion, chronic inflammation, and vascular injury, which may increase susceptibility to cognitive decline following chemotherapy. These mechanisms could partly explain the association observed in the present study.

In the present study, increasing chemotherapy cycles were significantly associated with poorer scores across all FACT-Cog domains, indicating that cumulative chemotherapy exposure adversely affected patient-reported cognitive function. Similar findings were reported by Durán-Gómez et al who observed significantly lower FACT-Cog scores across all cognitive domains among patients receiving four or more chemotherapy cycles.¹³ Singh et al observed a significant negative

correlation between the total number of chemotherapy cycles and the FACT-Cog total score ($r=-0.373$, $p=0.04$).⁷ They also demonstrated that a longer duration of chemotherapy was associated with poorer perceived cognitive abilities ($r=-0.482$, $p=0.006$), suggesting that prolonged treatment exposure contributes to worsening cognitive function.

In the present study, advanced cancer stage was significantly associated with poorer scores across all FACT-Cog domains, indicating worse patient-reported cognitive function among patients with more advanced disease. A similar observation was reported by Root et al who found that women with stage II/III breast cancer had lower FACT-Cog perceived cognitive impairment scores than those with stage 0/I disease, suggesting that greater tumor burden may contribute to cognitive difficulties even before the initiation of systemic therapy.¹⁴

These findings were further supported by the multivariable logistic regression analysis, in which advanced cancer stage and the number of chemotherapy cycles completed remained independent predictors of cognitive impairment after adjustment for potential confounding factors. In contrast, age, gender, body mass index, hypertension, ischemic heart disease, hypothyroidism, and chronic kidney disease were not independently associated with cognitive impairment. These findings suggest that treatment-related factors, particularly cumulative chemotherapy exposure and advanced disease stage, play a greater role in chemotherapy-induced cognitive impairment than demographic characteristics or most comorbid conditions.

Interestingly, type 2 diabetes mellitus was associated with lower odds of cognitive impairment in the present study. This finding is in contrast to previous studies. Sastre et al reported that type 2 diabetes is consistently associated with an increased risk of cognitive impairment and dementia, while Tabesh et al demonstrated that longer diabetes duration, poor glycaemic control, and hypoglycaemia further increase the risk of cognitive decline.^{15,16} The discrepancy observed in the present study may be related to differences in patient characteristics, glycaemic control, antidiabetic medications, or residual confounding. Therefore, this finding should be interpreted with caution and requires confirmation in larger prospective studies.

There are some limitations in the present study that should be taken into consideration. First, the cross-sectional design does not allow the evaluation of change in cognitive function over time and does not prove causality between chemotherapy and cognitive impairment. Second, the study took place at a single tertiary care centre and limit the generalisability of the findings to other settings. Objective neuropsychological testing was not conducted. Furthermore, the cognitive effects observed may be affected by the diversity in patients' cancer type and chemotherapy treatment. Further multicentre prospective studies incorporating both patient-reported and objective

cognitive assessments are needed to validate these findings and better understand the long-term effects of chemotherapy on cognitive function.

CONCLUSION

More than one-third of patients who received chemotherapy experienced chemotherapy-induced cognitive impairment. Advanced cancer stage and a greater number of chemotherapy cycles were identified as independent risk factors for cognitive impairment. The results of the study underscore the need for cognitive evaluations as part of the routine care of people undergoing chemotherapy, which would allow cognitive impairment to be identified early and supportive care to be provided promptly. Multicenter prospective studies are required to confirm these results and improve the management of chemotherapy-induced cognitive impairment.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Prasannan V, Joseph J, Teli SS, Akhtar S. Assessment of chemotherapy-induced cognitive impairment in cancer patients. *Int J Res Med Sci* 2026;14:4674-80.