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ASSOCIATION BETWEEN COGNITIVE IMPAIRMENT AND THE TYPES OF CANCER

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ABSTRACT
Cancer-related cognitive dysfunction has been described as a significant limiting factor in cancer patients and survivors quality of life. Cancer therapy is crucial in the treatment of various cancers such as sarcoma, breast cancer, colon cancer, head and neck cancer, and so on. However, it may also be a double-edged sword; research from various studies shows that certain cancer patients experience cognitive dysfunction after undergoing chemotherapy. Due to the fact that many patients are unaware of the cognitive side effects of cancer treatment, clinical recognition of Cancer-related Cognitive Impairment (CRCI) may be the most important aspect of its management and oncology care plan. For the assessment of cognitive dysfunction, MoCA is a neuropsychological battery scale that is superior to other battery scales of greater sensitivity and accuracy.

Keywords*: Assessment, Cancer, Chemotherapy, Cognitive impairment, Treatment.*

INTRODUCTION

When a person has trouble remembering, learning new knowledge, concentrating, or making decisions that affect their everyday lives, they are said to have a cognitive impairment. The severity of cognitive impairment ranges from mild to severe. Mild impairment can cause changes in cognitive functions, but people can still go about their everyday activities. Significant impairment levels can lead to a lack of ability to grasp the meaning or importance of something, as well as the ability to speak or write, making it impossible to live independently [1]. The chances of cancer patients, particularly those with metastatic disease, surviving have significantly increased thanks to advances in oncology diagnostic and therapeutic approaches. According to the GLOBOCAN project1 of the International Agency for Research on Cancer, India's cancer burden will nearly double in the next 20 years, from slightly more than a million new cases in 2012 to more than 17 million by 2035 [2]. Cancer-related cognitive impairment (CRCI) is common in patients treated for non-central nervous system cancers, particularly during and after chemotherapy [3]. Furthermore, some prospective longitudinal studies have shown that some cancer patients have impairments right before surgery, implying that the cancer itself is to blame [4]. Anaemia caused by chemotherapy has been related to a decrease in functional status and cognitive ability. Anaemia treatment or maintenance may help elderly cancer patients maintain functional independence while still shielding them from mental deterioration. It was found that higher Hb values were significantly associated with more favourable values for all indices measuring mental and functional capacity, depression, and co morbidity [5]. When compared to standard face-to-face Virtual Reality Rehabilitation (VRRS) treatment, there was an improvement in memory, language, and visuo-constructional abilities after the end of face-to-face VRRS treatment. The use of home-based cognitive VRRS tele therapy seems to cause more preservation of improvements than home-based unstructured stimulation [6].Chemotherapy-related cognitive impairment (CRCI), also known as cognitive dysfunction, chemo fog, or chemo brain, is a decrease of a number of neuropsychological behaviours in patients with non-central nervous system cancers following chemotherapy or other anticancer treatments such as radiation therapy or surgery [7]. The term is used to describe a group of cognitive disabilities that cancer survivors experience. The same disorder is also known as 'chemo brain' or 'chemo fog,' although the terminology implies that chemotherapy drugs are the cause of both short- and long-term cognitive impairments. While chemotherapy is known to have a negative impact on cognition, radiation therapy and adjuvant hormone therapies can also have a negative impact. Chemotherapy-related cognitive impairment (CRCI) affects 17–75 percent of cancer patients who receive chemotherapy [8]. It has been estimated that 18% of all breast cancer patients undergoing standard-dose chemotherapy have cognitive issues after treatment, with over 30% of patients evaluated two years after high-dose chemotherapy having such problems [9]. MCI affects 10-20% of adults over the age of 65; risk increases with age, and men tend to be at higher risk than women[60] .Around 58 percent of primary brain tumours are cancerous. Around 58 percent of primary brain tumours are cancerous [10]. Lung, breast, and unknown cancers, melanoma, and colon cancers are the most common primary cancers that cause brain metastasis [11].

DOMAINS OF COGNITIVE FUNCTION

Cognitive function is a general concept that encompasses mental processes such as knowledge acquisition, information manipulation, and reasoning. Perception, memory, learning, concentration, decision-making, and language skills are all examples of cognitive functions. Throughout recovery and survivorship, patients may go through a number of mental shifts. In non-CNS cancers, the severity of these changes is usually mild to moderate. [12]

Domains of cognitive function

Cognitive Domain	**Cancer-related Cognitive Impairment Presentation**	**Definition**
Attention and working memory	Patients with CRCI may experience "spacing out," difficulty focusing or multitasking, and trouble recalling phone numbers, lists, or names, among other symptoms.	focused awareness on a select subset of perceptual information; very shortterm memory used for immediate conscious processing
Processing speed	Patients may report that it takes them longer to process new information and complete routine tasks.	ability to automatically and fluently perform simple motor and cognitive tasks; a measure of cognitive efficiency
Executive functioning	Patients can have difficulty multitasking, preparing, and coordinating their lives.	Command and control of all cognitive skills; a sort of conductor of general processes
Learning and memory	Patients may complain about having difficulty learning new content, missing names or events, or having difficulty "finding" the correct phrase.	ability to acquire, retain, and efficiently retrieve new information

TYPES OF MCI

Amnestic MCI (a-MCI) patients are the most vulnerable of the MCI subtypes. [13] In amnestic MCI, memory is severely harmed. Some aspects of the brain are unchanged. Amnestic MCI is believed to be caused by Alzheimer's disease. In non-amnestic MCI, memory is unaffected, but one (single domain) or more (multiple domain) cognitive abilities (e.g., vocabulary, visual-spatial skills, and executive function) are impaired. In single domain MCI, only memory or one other field of cognition is impaired. In some domains of MCI, memory and one or more other cognitive abilities are affected. [14, 15]

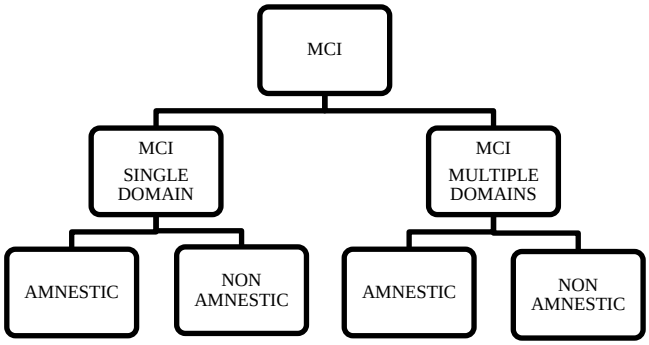

Figure: 1. MCI Types

EPIDEMIOLOGY

According to the GLOBOCAN project1 of the International Agency for Research on Cancer, India's cancer burden will nearly double in the next 20 years, from slightly more than a million new cases in 2012 to more than 17 million by 2035 [16]. In an epidemiology report, It was discovered that the overall administrative prevalence rate of dementia for people over 65 years was 9.3%. The reported prevalence for those in hospitals was 16.7%.Dementia patients had 33 percent more admissions, 36 percent more hospital days, and 18 percent higher costs per person-year than the control group [17]. Also after accounting for population cohort differences, it was discovered that cancer patients had a higher SCI prevalence and experienced more severe SCI than non-cancer controls [18]. MCI affects 10% to 20% of adults aged 65 and up; the risk of developing MCI rises with age, and men tend to be at higher risk than women [19]. It has been estimated that 18% of all breast cancer patients undergoing standard-dose chemotherapy have cognitive issues after treatment, with over 30% of patients evaluated two years after high-dose chemotherapy having such problems [20]. There is some evidence that women who have been treated for cancer have a higher incidence of cognitive decline than men [21]. MCI affects 10- 20% of adults over the age of 65; risk increases with age, and men tend to be at higher risk than women [22].

PREDISPOSING FACTORS

The chemotherapy-treated group showed significant reductions in FA in the frontal, parietal, and occipital WM tracts after treatment. Most chemotherapeutic agents are thought to not cross the blood–brain barrier (exceptions include methotrexate and 5-fluorouracil) (exceptions include methotrexate and 5-fluorouracil) [23] Recent reviews, however, have indicated that virtually all commonly used chemotherapeutic agents can cause central nervous system (CNS) disorders, such as encephalopathy, leukoencephalopathy, ototoxicity, and cerebellar symptoms [24] .Chemotherapy at high doses is more likely to affect cognitive performance than chemotherapy at lower doses [25].

The systemic effects of pro-inflammatory cytokines are linked to fatigue, depression, and cognitive decline, which can influence quality of life before, during, and after treatment [26]. Pro-inflammatory cytokines can infiltrate the central nervous system as a result of inflammation and interact with a cytokine network in the brain, affecting virtually every aspect of brain function linked to behaviour, such as neurotransmitter synthesis, neuroendocrine function, synaptic plasticity, mood-regulating neurocircuits, motor activity, motivation, anxiety, and alert. Cytokines may cause local inflammation in the brain via oxidative and nitrosative processes, especially in the hippocampus and other brain regions with high cytokine receptor density.

As a result of these responses, clinical signs of cognitive dysfunction, such as lapses in memory, concentration, processing speed, and response speed, will emerge [27]. While patients with poorer response speed output and perceived cognitive disturbances had higher levels of IL-6 and IL-1, IL-4 can protect against chemotherapy-related cognitive impairment [28].

The behavioural consequences of these immune system effects on the brain include depression, anxiety, fatigue, psychomotor deterioration, anorexia, cognitive dysfunction, and sleep impairment; symptoms that are similar to those described in neuropsychiatric disorders, especially depression. Pathways containing cytokine signalling molecules such as p38 mitogen-activated protein kinase and nuclear factor kappa B; indoleamine 2,3 dioxygenase and its downstream metabolites kynurenine, quinolinic acid, and kynurenic acid; neurotransmitters such as serotonin, dopamine, and glutamate; and neurocircuits involving basal ganglia and anterior cortex [29]. AraC causes neuronal apoptosis by inducing the formation of reactive oxygen species, causing oxidative DNA damage, and initiating the p53-dependent apoptotic programme [30].

Peripheral cytokines can directly penetrate the blood-brain barrier via active transport mechanisms or indirectly via vagal nerve stimulation. . In animals and humans, peripheral administration of such cytokines as biological response modifiers causes adverse cognitive effects [31]. Adjuvant chemotherapy-induced decreases in reproductive hormone levels, especially estrogens and progesterone can play a role in the decline of cognitive function [32]. The results suggest that there are subgroups of people with different attention function trajectories, as well as a genetic link to IL6 promoter polymorphism [33].

Endogenous levels of cytokines including tumour necrosis factor may be influenced by ADR (TNF) circulation of ADR-induced the observed CNS damage associated with this cancer chemotherapy agent is causally linked to TNF. TNF-induced mitochondrial dysfunction causes an increase in oxidative stress in the brain, which has cascading effect [34] .The findings point to subgroups of people that have different attentional function trajectories, as well as a genetic similarity to the IL6 promoter polymorphism [35].

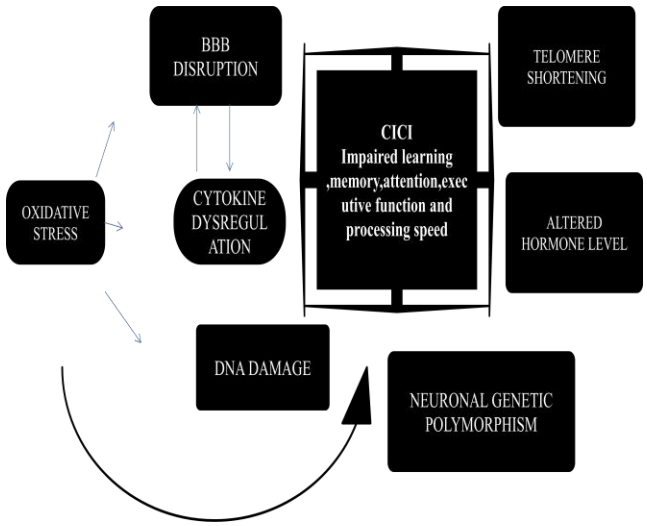

Figure: 2. Pre-disposing factors for CI

EVALUATION OF COGNITIVE IMPAIRMENT (NEUROPSYCHOLOGICAL BATTERY SCALES)

Accurate assessment is essential for developing effective strategies. Instruments including the Mini-Cog, Memory Impairment Screen (MIS), and General Practitioner Assessment of Cognition (GPCOG) have all been consistently recognised for their utility in primary care. As a result of sensitivity improvements, frontal/executive functioning, and reducing exposure to cultural and educational prejudices, the clock drawing test (CDT) and newer approaches such as the Montreal Cognitive Assessment (MoCA) and the Rowland Universal Dementia Assessment Scale (RUDAS) are gaining credibility [36]. Several of the illustrated screening measures are as follows:

MoCA: The MoCA is a 10-minute, 30-point cognitive screening test designed to aid health practitioners in detecting MCI in patients with an MMSE score of 24 to 30 points. 26. The (MoCA) 26 is the suggested cut-off point. The (MoCA) is Frontal executive functioning tasks are receiving more attention.) The MoCA is a widely used screening method that takes about ten minutes to complete. Skills related to visual perception, focus, language, reasoning, executive function, delayed memory, and direction are all assessed. This can make it more sensitive to non-AD dementia and attention detection than the MMSE [37]. The MoCA is a brief cognitive screening tool with high sensitivity and specificity for detecting MCI, as it is currently conceptualised in patients living in the normal range on the MMSE [38, 39, 40].

Montreal cognitive assessment includes the following:
Alternating trial making(0-1)
visuoconstructional skills (cylinder) (0-1)
naming (0-3)
attention(0-2)
vigilance(0-1)
serial 7s(0-3)
sentence repetition(0-2)
verbal fluency(0-1)
abstraction (0-2)

delayed recall(0-5)
orientation (0-6)
Completing 12 years or more of formal education earned an additional point.

MMSE: The Mini Mental State Examination (MMSE) is a cognitive test that is often used to screen for dementia. [41] Dementia is a condition that causes progressive global cognitive decline. Some people with mild cognitive impairment (MCI) develop dementia, while others stay stable or regain full function. Finding strong predictors of dementia in people with MCI is a hot topic. In clinical, academic, and community settings, the Mini-Mental State Examination (MMSE) is the most well-known and widely used brief screening method for providing an overall measure of cognitive impairment [42]. Because of its accuracy and brevity, the MMSE-S can help to improve the cost-effectiveness and accessibility of dementia screening, as well as early diagnosis and treatment of dementia, particularly in low- and middle-income countries [43]. The researchers concluded that the MMSE provides a valid diagnosis of cognitive impairments in people with moderate and severe dementia in general populations. MMSE, on the other hand, is not recommended as a screening method for the diagnosis of early stages of dementia [44]. The MoCA test meets the requirements for screening tests for MCI identification in patients over 60 years of age better than the MMSE test [45].

Mini-Cog: The Mini-Cog outperformed the MMSE in identifying MCI patients, according to (Li X et al.). Mini-Cog had a smaller impact on age and education levels than the MMSE. The Mini-Cog test was simple (3-4 minutes) and well received by the patients. Primary hospital outpatient departments could benefit more from Mini-Cog [46].

Memory Impairment Screen: The memory impairment screen (MIS) is a quick test that can determine whether or not you have a memory problem. As a preliminary test, it's often used in combination with other screening approaches. The MIS holds true across a wide range of cultural environments and languages. It does not assess executive functioning, which in some cases may be a symptom of dementia such as vascular dementia and fronto temporal dementia. It does not measure visuospatial capacity, which can also be harmed by dementia [47].

GPCOG: The General Practitioner Assessment of Cognition (GPCOG) consists of a series of cognitive tests as well as questions about the informant's background. In primary care, the GPCOG is a reliable, inexpensive, and commonly used dementia screening method [48].

SLUMS: The SLUMS isn't yet another screening tool to add to the already long list of cognitive tests used in Polish clinical practise; statistical research shows that it outperforms the MMSE, Poland's most widely used scale, in terms of screening diagnosis [49].

CANCER TYPES AND COGNITIVE IMPAIRMENT:

Breast Cancer: The majority of chemotherapy patients suffer from cognitive impairment, such as memory, comprehension, concentration, and thought issues. The most commonly prescribed chemotherapeutic drugs for lung and breast cancer are doxorubicin and cisplatin. According to studies, both drugs have the potential to cause chemo brain [50]. While hormonal therapies are commonly used to treat breast cancer, few studies have looked into the potential cognitive effects. Anti-oestrogen therapy can induce a particular verbal memory impairment, corroborating the links between oestrogen levels and verbal memory that have been identified in studies of hormone replacement therapy's cognitive benefits [51]. Exercise is proven to enhance brain function. Patients with different cancers, including breast cancer, can benefit from low-intensity exercise to prevent cognitive impairment during or after chemotherapy [52]. A Cognitive impairment can have a significant impact on breast cancer survivors' health-related quality of life [53]. When their cognitive capacity was checked, more than 90% of the patients treated with adjuvant therapy had gone through chemotherapy-induced menopause, and about 40% were taking tamoxifen [54].

Head and Neck Cancer (Hnc): In the United States, head and neck cancers account for less than 5% of all cancers and less than 3% of all cancer deaths. People who have a long history of smoking and consuming alcohol are at risk for head and neck cancers [55].Owing to illness, care, and lifestyle causes, newly diagnosed patients with head and neck cancer may be at risk for diminished neurocognitive function (NCF) [56]. Patients who received cisplatin tended to have worse objective Cognitive function than those who only received Radiation Therapy [57]. Patients with head and neck cancer are more likely to experience functional and cognitive disability, depressive symptoms, and social isolation, all of which are linked to a higher risk of poor health outcomes [58, 59]. In patients with HNC, cognitive impairment is normal, and there are significant links between cognitive impairment and psychosocial, QoL, and treatment adherence variables [60].

Cervical Cancer: According to population-based registries, cervical cancer is on the decline in India, but it remains a major public health issue for Indian women. Cervical cancer is most common in women between the ages of 55 and 59, and a large percentage of those diagnosed are in advanced stages of the disease [61]. Since undergoing chemotherapy, patients with gynaecological cancer had lower neurocognitive test scores and improved functional network studies [62]. The structural networks in the brain may be disrupted as a result of cisplatin-based chemotherapy. Impaired brain networks in chemotherapy patients may lead to decreased performance over time on both specific and nonspecific cognitive functions [63]. Improved understanding of cognitive complaints could lead to the creation of appropriate clinical strategies for prevention and the provision of supportive care services, such as educational and counselling services, to help women with cervical cancer minimise cognitive disability.

Colorectal Cancer (CRC): Chemotherapy patients reported the most cognitive symptoms [64] CRC patients have a three to five times higher prevalence of cognitive disability than Head Cancer (HC) patients, with women having a higher rate

of impairment than men [65]. Since receiving oxaliplatin/fluorouracil chemotherapy, patients with CRC had their cognitive function assessed in two single-arm trials. One study found no evidence of cognitive impairment, but it was constrained by a small sample size, the absence of a comparator group, the use of a brief cognitive battery, and the failure to account for practise impact [66].The other study found that participants had 37 percent to 39 percent cognitive impairment before and after chemotherapy, with 52 percent showing a decline from baseline, especially in verbal memory. Women with CRC had more cognitive disability than men [67].

TREATMENT OPTIONS:

Chemotherapy and radiotherapy may cause cognitive dysfunction, which is a difficult side effect with little treatment options. CNS stimulants (e.g., methylphenidate and modafinil), drugs for patients with memory impairment (e.g. donepezil, memantine, and ginkgo biloba), and bone marrow stimulating agents are all pharmacotherapeutic options for cancer therapy-induced cognitive symptoms (e.g. erythropoietin) [68]. In other patient populations, brain stimulation techniques such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation have demonstrated beneficial effects on memory, mood, and fatigue, although they have yet to be tested in the context of CRCI [69].

Person or group outpatient therapy led by a trained clinician (neuropsychologist, psychologist, occupational therapist, or speech language therapist) is typically used in rehabilitation programmes with the goal of improving patient cognition and real-world functioning [70]. Self and organizational management by noting down ideas Focusing on one mission at a time Not in a hurry Allowing oneself to make mistakes is a kind of self-acceptance. Use of cues as a reminder Creating a schedule/routine. Erythropoietin is a naturally occurring glycoprotein that activates the development of red blood cells and is often used to boost haemoglobin levels in anaemic patients [71]. Vitamin E is a nutrient that works as an antioxidant, scavenging harmful free radicals. The discovery that free radicals may play a role in the pathological processes of Alzheimer's disease has sparked interest in using vitamin E to treat the disease. Vitamin E and C supplements can protect against vascular dementia and improve cognitive function in later life, according to findings [72]. Behavioural, nutritional, and exercise regimens have also been shown to help reduce behavioural and cognitive symptoms [73]. People who are physically active will benefit more from cognitive stimulation than those who are not.

DISCUSSION

Since many patients are unaware of the cognitive side effects of cancer care, clinical recognition of CRCI and developing an oncological treatment plan is likely the most critical aspect of managing it and developing an oncological treatment planis likely the most critical aspect of managing it and developing an oncological treatment plan. Caregivers play an important part in the treatment of cancer patients.According to some reports, however, caregivers have far more unmet needs than patients. Early supportive treatment, directed not only at patients but also at caregivers, can improve this population's quality of life (QoL) [74]

Form a partnership with caregivers.

Both caregivers and patients should be evaluated.

Encourage patient–caregiver collaboration by using three-way contact.

Provide assistance and facts.

Consult with departments and blogs.

Encourage family contact to continue.

Encourage active coping.

To resolve cognitive changes after cancer, oncology nurses must understand the available evidence and offer knowledge and advice to cancer survivors. Clinicians must expect that cognitive dysfunction can interfere with patients' everyday functioning (e.g. treatments or job-related decision making) [75]. Clinical support may help caregivers see the bright side of their situation and retain a rational sense of hope.

CONCLUSION

Cancer-related cognitive impairment is known to occur often, but its precise nature is unknown because different study methodologies and criteria such as assessment of cognitive dysfunction, MoCA is a neuropsychological battery scale that is superior to other battery scales of greater sensitivity and accuracy have been employed to measure different aspects of these patients cognitive performance.The majority of research has found that the cognitive domains most frequently affected by cancer and cancer-related treatments include concentration, recall, and information processing;but did not have a history of mood disorder. Therefore, further study is obviously required.

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