Original Research Article

A study on prevalence of cognitive functions impairment in advanced breast cancer patients in referral hospital at Hyderabad

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Abstract

Background : Cognitive impairment is the most frequent complication experienced in advanced breast cancer patients Patients often develop cognitive problems as impairment in memory and verbal fluency, slowing down of thought processes, and a decrease in their attention span, If untreated, will impair their performance at work and home and eventually diminish an individual's quality of life .**Aim of the study:** To study cognitive functions in advanced breast cancer patients**Materials & methods:** A cross sectional study was done in the department of psychiatry, for a period of one year in 30 patients and 30 controls who fulfilled the inclusion criteria and exclusion criteria were selected by purposive sampling technique and socio-demographic data was collected. Cases of breast cancer involving administration of a battery of neuro-psychological tests to assess the cognitive functions in patient group and control group which have been matched for age and socio-economic status.**Results**: There was significant difference between early (stages I & II) and late (stages III & IV) breast cancer only in DSST TT (P=0.021) and DSST E (p=0.028). No statistical significant difference was noted on SMMSE and TMT B tests. The group of patients who were treated with chemotherapy did not statistically vary from the group who were not treated with chemotherapy on any of the cognitive tests.**Conclusion:** Analysis of data revealed 100 % subjective report of cognitive functioning among cases and controls in the domains of brief cognitive rating scale.

Keywords: Breast cancer , cognitive functions, subjective report

Introduction

Cancer-related cognitive impairment(CRCI) is the most frequent complication reported by breast cancer patients[1] and up to 75% of breast cancer patients experience CRCI during active treatments (e.g., chemotherapy and hormonal treatment).[2,3] Individuals with CRCI often characterize their cognitive problems as impairment in memory and verbal fluency, slowing down of thought processes, and a decrease in their attention span.[4,5] If unmanaged, CRCI will impair performance at work and home and eventually diminish an individual's quality of life (QoL).[6,7]CRCI could also progress to long-term cognitive impairment.[8].Older patients with breast cancer and with CRCI have 10% to 15% probability of developing dementia per year compared to about 1% to 2.5% among those without CRCI. [9] CRCI is defined as one or more impaired functions of interrelated cognitive process.[10] Patients with CRCI describe their condition as frequent forgetfulness(e.g., names, date, or telephone numbers), slow-progressing speeds, and difficulties in concentration, multitasking, and word retrieval.[11] In most cases, breast cancer patients seldom anticipate that they will have to deal with CRCI during the illness trajectory of cancer.[7] This unexpected event leads to frustration and embarrassment in breast cancer patients.[7]CRCI can be classified as subtle, moderate, and severe using scores obtained from neuropsychological testing. Based on criteria developed by Vardy *et al*., subtle CRCI is defined as −1 to –1.49 standard deviation (SD) below population normative means; −1.5 to −1.99 SD below the normative means can be defined as moderate CRCI, and equal and below −2 SD is defined as severe CRCI.[12]Using these criteria, 11%–27% breast cancer patients who are recovering from surgical removal for their breast cancer were found to have moderate or severe impairment on verbal fluency and 14%–17% complained of memory impairment.[5]

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Aims & Objectives

To study the psychiatric cognitive functions in diagnosed breast cancer patients.

Materials and Methods

Cross sectional study, involving two study groups for a duration of one year ie**,** from January 2014 to June 2015. At Osmania Medical College Allied Hospitals (M.N.J Institute of Oncology & Regional Cancer Centre for Cases and Osmania General Hospital for Controls),Hyderabad,Telangana. There were no ethical issues in our study . Written informed consent was taken form all the patients with advanced breast cancer were included in the study

Inclusion Criteria: Age 20-60 years of female sex, who are diagnosed with breast cancer **,** Matched for age and socio-economic status to the subject sample for controls.

Exclusion Criteria: Age > 60 years **,** Pre existing neuropsychiatric, neurodegenerative disorder and other significant medical disorders which may influence cognitive function, Individuals with substance abuse / dependence disorder, Individuals suffering from any sensory impairment that is visual or hearing impairment or learning disability which may serve as a hindrance in performing the tests.

Method of collection

Cases of breast cancer involving administration of a battery of neuro-psychological tests to assess the cognitive functions in patient group and control group which have been matched for age and socio-economic status.30 patients and 30 controls who fulfilled the inclusion criteria and exclusion criteria (which are stated below) were selected by purposive sampling technique and socio-demographic data was collected. All patients were diagnosed by the

oncosurgeonA written informed consent was obtained from all the patients, who were prior to consent, informed that refusal to participate would not alter the course of treatment nor would affect the outcome.

Instruments for assessment of cognitive functions:

Standardized mini mental status examination. (SMMSE)
Brief cognitive rating scale (BCRS)
Trial making test B
Digit symbol substitution test (DSST)

Instrument for assessment of socioeconomic status

Modified BG Prasad 2014 scale.

Description of the Tools

This proforma is especially designed for this current study. It deals with Name, Age, OP no., IP no., marital status, Religion, Address, Domicile, educational status, occupation income.This is followed by the clinical history containing the diagnosis (stage of breast cancer), duration of illness, treatment history, medical and psychiatric co-morbidity, habits, significant family history. The current medication is also noted.The scores of SMMSE, BRCS, TMT-B, DSST, GHQ – 28, Mini-plus AND Modified B.G. Prasad 2014 scale can be written in a tabulated form in the proforma.

SMMSE

The SMMSE is a bed side screening test for cognitive impairment , derived from the MMSE , developed by Folstein, which is the most widely used instrument to measure cognitive impairment. SMMSE was attempted to build on the advantages of MMSE namely ease of administration and scoring while addressing its shortcoming viz rater inter rater variance.SMMSE is administered by a trained rater or clinician and takes about 5- 10 minutes. It contains 12 items which are asked in sequence to generate a total score of 30. The scores of less than 18 indicate severe cognitive impairment while 18-23 point to a mild impairment and scores above 24 is reflective of no impairment. Questions that are not answered should be treated as errors. The SMMSE is brief, easy to use and can be administered by non professionals to measure cognitive functioning in adults. SMMSE has clearer instructions than MMSE and has time limit for the answers, commensurate with the cognitive tasks.It has good content and concurrent validity and is organized into discrete subsections measuring orientation, registration, attention and concentration, recall, language and construction. It also has spell the WORLD backwards and the score is total 5.But the subsections and individual items cannot be viewed as measures of specific aspects of cognition, because of factor analytic studies typically yield a two factor solution. Because of the non specific nature of the individual subsection scores of SMMSE, it should be followed by a more comprehensive assessment, as attempted in the current study.

Brief Cognitive Rating Scale (BRCS)

BRCS is designed specifically to assess the syndrome of cognitive decline. As a clinical rating instrument, BRCS merges the judgement and skill of the clinician with objective rating criteria. Consequently, stable data can be obtained on subjects with cognitive impairment who may be only variably co-operative and attentive. BRCS assesses the magnitude of cognitive impairment on 5 clinical axes, each scored on a Likert scale of 1 to 7 using specified criteria. The axes represented are concentration, recent memory, orientation and functioning. Items are scored on the basis of a structured clinical interview conducted in the presence of primary care giver. The BRCS (Part 1) differ from virtually all other presently used clinical instruments for cognitive disturbances in that it includes mood changes such as depression, anxiety, agitation and psychosis. Thus the effects of interventions on cognition and associated functioning can be specifically assessed. BRCS is a part of the trial of assessments with global deterioration scale and functional assessment staging.

Trial Making Test Part B (TMT-B)

TMT originally constructed in 1938 as "Partington's Pathways" or "Divided Attention Test" is a timed test of speed for attention, sequencing, mental flexibility, visual search and motor function. TMT is available in various formats, namely TMT – Part A and Part B, oral Trial Making test and color trail test.

TMT - Part A requires connection, by making pencil lines between 25 encircled numbers randomly arranged, in a proper order while Part B has 25 encircled number and letters in alternating order. Scoring is expressed in terms of time in seconds required to complete the test. Errors are recorded and the subject continues with the test. Scores are strongly influenced by age, education and intelligence of the subjects. Interpretations of scores are based on normative data.

TMT Part B is associated with the processes of distinguishing between numbers and letters, integration of two independent series, ability to learn an organizing principle and apply it systematically, reveal retention and integration, verbal problem solving and planning. It is a useful tool in identifying general frontal lobe dysfunctions by indicating an inability to execute and modifying aplan of action.

.**Digit Symbol Substitution test (DSST)**

It is a test of visuo-motor co-ordination, motor persistence, sustained attention and response speed. Rapid information processing is required in order to substitute the symbols accurately and quickly.The test consist of a sheet in which number 1-9 are randomly arranged in 4 rows of 25 squares each.The subjects substitute each number with a symbol using a number symbol key given at the top of the page. The time taken to complete the test in seconds forms the score and errors are noted down. It requires combining the newly learned number or symbol pairs, accurate visual perception, appropriate age co-ordination, short term memory and ongoing processed attention. This test is extremely sensitive to cognitive deterioration. It is affected by age and by impairment of visual performance.

General health questionnaire -28 (GHQ-28)

The 28 item scaled version of General Health Questionnaire (GHQ) GHQ-28 is ascreening device, developed by Goldberg, for identifying minor psychiatric disordersin the general population and within community or non-psychiatric clinical settingssuch as primary care or general medical out-patients. Suitable for all ages fromadolescent upwards – not children, it assesses the respondent's current state andasks if that differs from his or her usual state. It is therefore sensitive to short-termpsychiatric disorders but not to long-standing attributes of the respondent. Itassesses somatic symptoms, anxiety and insomnia, social dysfunction and severedepression.

Mini International Neuropsychiatric Interview- plus (mini- plus):

This is a structured diagnostic interview developed by Sheehan et al for diagnostic psychiatric disorder as per DSM-IV and ICD – 10 diagnostic criteria. Itincludes 26 modules. It features question on rule outs, disorder sub-typing andchronology (e.g. age at onset). It also features a number of algorithms to handlepsychotic disorder and hierarchical rule outs in the event the patient had more thanone disorder at a time. MINI plus has a good reliability and validity in elicitingsymptom criteria used in making DSM-IV and ICD – 10 diagnoses and is comparablewith that of SCID-P and CIDI, The English version 5.0.0 of MINI plus was used for the currentstudy. The modules for conduct disorder, attention deficit hyperactive disorder (children /adolescents) were omitted as the study sample included only those aged 60 years and above. Patients were assessed with the MINI – screen and the positive modules were evaluated in detail. The MINI – screen and the MINI-plus take around 5-10 minutes and 20-30 minutes to complete respectively.

Modified BG Prasad scale (2014) is a commonly used scale to measure the socioeconomic status of families. The advantages of using this scale are: It is applicable to both urban and rural areas and, therefore, uniformity is maintained, and it can be used to compare across these regions. Also, it utilizes the per capita monthly income and is therefore applicable to individuals. On the other hand, its most important disadvantage is that it takes into account only the income and, therefore, may miss out on the other factors affecting the social

status of the individual. Nevertheless, it remains one of the most widely used scales to determine the socioeconomic status in health studies due to the ease of application.The revised income categories for January 2014 for all India have been given in the table. They have been computed using the AICPI for January 2014 as 237.

Statistical Methods

The study as well as control subjects were tested for cognitive functions using SMMSE, BRCS, TMT – B and DSST. The various findings were analysed using Chi-square test and T test.

Results

A total of 60 subjects, 30 breast cancer patients (cases) and 30 matched women not suffering from cancer (controls) were included in the study.Patients in the age group of 41-50 years of age constituted the major part of the cases (46.7%) and individuals in the age group of 31-40 years constituted the major part of control group(60%) followed by patients in age group of 41-50 years (33.3%).There was no significant difference between the age of cases and control group ($p > 0.05$). Age was not a confounding factor in the statistical assessment.Among the cases 22 were married, 2 were single, 2 were divorced/separated and 4 were widowed. Among the controls 25 were married, 3 were separated/ divorced and 2 were widowed. There was no statistically significant difference between marital status of cases and controls ($p = 0.453$).There was statistically significant difference between the cases and controls in their place of residence ($p=0.043$).

In cases, maximum constituted of rural dwellers (46.7 %)followed by 43.3% in semi urban areas and 10 % in urban areas. Among the controls, semi urban dwellers were 70% forming the largest group, rural dwellers 16.7 % and urban dwellers were 13.3 %. The difference was not highly significant. It could be because the controls, who were bystanders of patients in medical wards were residing more in the semi urban areas.The largest group in cases as well as control group was Hindus (63.3% of cases and 50% of control group) followed by Christians and Muslims. There was no significant difference between the control group and cases in religion ($p=0.381$).60 % participants had completed their primary schooling. 33.3 % of cases and 36.7 % of controls were educated up to High School. 6.7 % of cases and 3.3 % of controls had attended college. There was no significant difference between control group and cases. Unskilled labourers formed the largest group in both cases and controls (93.3% and 83.3% respectively). There is no significant difference in occupational data between cases and controls ($p = 0.316$ Most of the cases (80%) as well as controls (90%) belonged to the socioeconomic status III. There was no statistical significant difference between cases and controls ($p=0.248, > 0.05$).The duration of illness was noted to be < 1 Yr in most of the patients(63.3%). Maximum no. of patients had undergone surgery and chemotherapy (43.3 %).Analysis of data revealed 100 % subjective report of cognitive functioning among cases and controls in the domains of brief cognitive rating scale. Subjectively cases did not report of any cognitive impairment.

Table 1: Trial Making Test Part B

	Group	N	Minimum	Maximum	Mean	Std. Deviation	t value	d.f	p value
TMT B – TT (sec)	Cases	30	150	780	375.17	147.960	2.542	58	.014
	Controls	30	150	480	294.17	92.504			
	Total	60	150	780	334.67	128.975			

There was significant difference ($p = 0.014$) between the cases and control group in the mean time taken to complete the trial making test. Results show significant cognitive impairment in cases.

Table 2: Trial Making Test Part B (errors)

	No. of errors	Group		Total
		Cases	Controls	
TMT B - E	1	12	7	19
	2	1	2	3
	3	1	1	2
	4	0	1	1
	6	1	0	1
Total		15	11	26

In the trial making test, most of the cases made a single error (80%), likewise among the control group also , single errors were committed by (63.6%) most of the individuals.There was no statistically significant ($p = 0.758, > 0.05$) difference between control group seen.

Data Analysis revealed no significant difference ($p=0.412, > 0.05$) between the control group and the cases in the mean time taken to complete the Digit Symbol Substitution Test.No significant difference ($p =1.00$) between the case and control group is seen in the mean no. of errors made on the Digit Symbol Substitution Test.

Table 3:Duration of illness Vs cognitive function

Test	Group	Duration	N	Min	Max	Mean	SD	t	P
Total score SMMSE	Cases	< 1 yr	19	25	30	28.47	1.504	0.665	0.512
		>1 yr	11	27	30	28.82	1.079		
			30	25	30	28.60	1.354		
TMT TT (in sec)	Cases	< 1 yr	19	150	720	353.68	141.841	1.047	.304
		>1 yr	11	195	780	412.27	157.740		
			30	150	780	375.17	147.960		
TMT E	Cases	< 1 yr	9	1	3	1.22	.667	1.096	.293
			6	1	6	2.00	2.000		
			15	1	6	1.53	1.356		
DSST TT (in sec)	Cases	< 1 yr	19	330	840	572.63	121.637	.663	.513
		>1 yr	11	360	780	541.36	129.462		
			30	330	840	561.17	123.279		
DSST E	Cases	< 1 yr	3	1	3	1.67	1.155	.178	.870
		>1 yr	2	1	2	1.50	.707		

			5	1	3	1.60	.894		

When duration of illness was compared with cognitive functions, no statistical significance was noted on SMMSE, TMT B and DSST measures. Results indicate no relation of duration of illness with cognitive functioning.

Table 4:Stage of breast cancer Vs cognitive function

Test	Group	Stage ofBreast cancer	N	Min	Max	Mean	SD	t	P
Total score SMMSE	Cases	Early	19	25	30	28.95	1.079	1.031	0.064
		Late	11	27	30	28.00	1.612		
		Total	30	25	30	28.60	1.354		
TMT TT (in sec)	Cases	Early	19	150	780	359.74	170.860	.745	.463
		Late	11	240	585	401.82	98.521		
		Total	30	150	780	375.17	147.960		
TMT E	Cases	Early	8	1	3	1.25	.707	.857	.407
		Late	7	1	6	1.86	1.864		
		Total	15	1	6	1.53	1.356		
DSST TT (in sec)	Cases	Early	19	330	630	522.37	92.005	2.454	.021
		Late	11	360	840	628.18	145.039		
		Total	30	330	840	561.17	123.279		
DSST E	Cases	Early	3	1	1	1.00	-	4.025	.028
		Late	2	2	3	2.50	.707		
		Total	5	1	3	1.60	.894		

There was significant difference between early (stages I & II) and late (stages III & IV) breast cancer only in DSST TT (P=0.021) and DSST E (p=0.028). No statistical significant difference was noted on SMMSE and TMT B tests.

Table 5: Treatment modality vs cognitive function

Test	Group	Treatment	N	Min	Max	Mean	SD	t	p
Total score SMMSE	Cases	No Chemotherapy	11	26	30	28.45	1.368	.441	.662
		Chemotherapy	19	25	30	28.68	1.376		
		Total	30	25	30	28.60	1.354		
TMT TT (in sec)	Cases	No Chemotherapy	11	150	780	390.45	192.529	.424	.674
		Chemotherapy	19	240	720	366.32	120.218		
		Total	30	150	780	375.17	147.960		
TMT E	Cases	No Chemotherapy	3	1	3	1.67	1.155	.184	.857
		Chemotherapy	12	1	6	1.50	1.446		
		Total	15	1	6	1.53	1.356		
DSST TT (in sec)	Cases	No Chemotherapy	11	330	780	562.73	138.065	.052	.959
		Chemotherapy	19	360	840	560.26	117.868		
		Total	30	330	840	561.17	123.279		
DSST E	Cases	No Chemotherapy	2	1	1	1.00	-	1.342	.272
		Chemotherapy	3	1	3	2.00	.707		
		Total	5	1	3	1.60	.894		

The group of patients who were treated with chemotherapy did not statistically vary from the group who were not treated with chemotherapy on any of the cognitive tests.

Discussion

This study is a comparative study between breast cancer patients and non cancer individuals in the aspects cognitive functions. This study revealed that there is statistically significant cognitive impairment in breast cancer patients as compared to non cancer individuals.In the present study, the various socio-demographic data was matched for cases and controls. However a statistical significant difference was noted only for domicile data. This could be because the controls for the study were bystanders of medical ward patients who were mostly residing in the semi-urban areas.Meyers CA[13] observed that the cognitive dysfunctions like memory loss, distractibility, difficulty in performing multiple tasks (multitasking) and myriad of other symptoms are experienced by many cancer patients. The etiologies of these problems may include the direct effects of cancer within the central nervous system (CNS), indirect effects of certain cancers (e.g., paraneoplastic brain disorders) and both diffuse and highly specific effects of cancer treatments on the brain. These patients may have coexisting neurological or psychiatric disorders in addition to the cognitive dysfunction that effect their cognition and mood. Findings from studies of Mehnert et al 2007& Von Ah D et al suggest breast cancer patients who receive adjuvant chemotherapy are likely to experience some degree of cognitive dysfunction. These women also tend to report more cognitive problems[14,15].The use of a cross-sectional, between-subjects research design in which patients are assessed only after treatment completion is an important limitation of most of the studies which include the study of Donovan KA et al[16].The Mini Mental Status Examination (MMSE) developed by Folstein[17] has widely been used as a measure of cognitive function and has proven to be a reliable and valid indicator of cognitive functions. The current study used Standardized Mini Mental Status Examination (SMMSE) which is an improvement on MMSE. In the current study, the total score obtained was 28.60 and controls were 29.70.

There was highly significant statistical difference between cases and controls. A cut off score of less than 24 on MMSE is considered to indicate cognitive impairment. Though the mean score on SMMSE in cases is more than 24, highly significant differences were obtained in individual domains of recall and language, significant difference in the domain of orientation in cases when compared to controls. A study that used MMSE previously along with other cognitive screening tests has shown highly significant cognitive impairment in

breast cancer patients. Most studies including the study of Philips KA et al[18] have used extensive neuropsychological batteries for cognitive testing and have shown fairly global impairments, more so in memory, language, verbal memory and psychomotor functioning domains. An SMMSE is less than ideal in evaluation of mild cognitive impairment and is biased towards verbal items and does not adequately measure other cognitive functions like ability to attend to relevant input, ability to solve abstract problems, psychomotor speed and visuospatial ability, this study also assessed the subjects in further detail with BCRS, TMT – B, DSST which is one of the strengths of this study.Very few studies done so far have used BCRS to evaluate cognitive impairment in breast cancer individuals. This study has attempted to evaluate the cognitive function in the study subjects with BCRS. Analysis of data revealed 100 % subjective report of cognitive functioning among cases and controls. Subjectively cases did not report any report any cognitive impairment. Patients with breast cancer often complain of problems with their memory and concentration. Colloquially, this problem is referred to as "chemo brain"orchemofog. Subjective reports of cognitive dysfunction correlated with anxiety and depression but not with objective cognitive function.The lack of correlation between objective and subjective function in these studies suggests that patients complaints about their cognitive function may be more indicative of emotional distress than true cognitive dysfunction[19-21]. In this study patients did not subjectively report impairments in cognitive functioning when evaluated on the BRCS though there cognitive deficits on SMMSE which goes against the previous reports. This could be because the previous studies have used different scales than the BCRS like Squire Memory Self-Rating Questionnaire, EORTC QLQ-C30 cognitive sub scale which are not available for use in this study.Cognition considers various mental processes like attention, concentration, memory, orientation, abstraction, intelligence, reasoning, problem solving and executive functioning. SMMSE and BCRS don't evaluate all these areas adequately.Earlier studies including the study done by Jim HSL et al [22].have used tests like Rey Auditory Verbal Learning Test (for learning & delayed recall), Weschler Memory Scale – Revised (for memory), clock drawing (for executive functions), copying a box drawing (for visuospatial ability), California Verbal Learning Test (for Verbal Episodic memory), The Digit Span subtest of the Wechsler Adult Intelligence Scale – III , Spatial Span subtest of the WAIS –III,Trail Making Test, and Ruff 2 & 7 Test, The Conner's Continuous Performance Test (for attention). The Digit Symbol subtest of the WAIS-III, Trails B sub test of the Trial Making Test and the Controlled Oral Word Association (for Complex cognition [15,22].These tests couldn't be applied in current study due to certain practical issues like the limited period of study. The cognitive functions noted to be impaired were verbal learning, memory function, reaction time, attention, learning & processing speed [23,24].The advantage of these tests is that they detect subtle and circumscribed pockets of cognitive impairment in the subjects. To overcome this drawback, 2 domain specific tests TMT-B and DSST have been used to comprehensively assess cognitive function – which is a notable strength of this study.TMT-B is a test frequently employed in previous studies also. It is a test of attention, visual scanning, sequential abilities and executive function. TMT-B has revealed significant ($p=0.014$, < 0.05) difference between cases and controls as far as time taken to complete the test is concerned. However no significant difference was noted in the number of errors made by both the groups.TMT-B is more sensitive to cognitive dysfunction than SMMSE and hence its use helps to detect subtle cognitive decline which is another strong point of this study. DSST is a timed test of attention, psychomotor performance and perceptual organization. There was no significant difference in time taken to complete the test and no. of errors made, between cases and controls. The current study shows deficits in recall, language, attention, executive function, visuospatial functions in the breast cancer subjects, which are consistent with earlier studies[18,19,23,24]. Orientation domain has not been recorded to be affected in previous studies and is new finding in this study.On DSST , there was no significant difference in time taken to complete the test and no. of errors made, between cases and controls. Cognitive functioning was also compared among patients treated with and without chemotherapy and no significant difference was noted among the groups. Two of the studies are in favour of these finding[16].Hurria A et al(2006) have conducted a neuropsychological testing before chemotherapy and 6 months after chemotherapy in 28 women aged 65 and older with stage I to III breast cancer. The following domains of cognitive functions were examined, attention, verbal memory, visual memory and verbal, spatial, psychomotor and executive functions. 14(50%) had no change, 11(39%) worsened, and three (11%) improved (P=.05). seven patients (25%) experienced a decline in cognitive function, defined as a 1-SD decline from pre to post testing in two or more neuropsychological domains[25].On DSST , there was no significant difference in time taken to complete the test and no. of errors made, between cases and controls. The findings of the current study could be explained on the basis of smaller sample size in this study as well as the patients of no chemotherapy group getting some other modality of treatment like radiotherapy, hormonal therapy which could have also affected their cognitive functioning.In the studies that have compared cognitive functioning in breast carcinoma patients treated with or without chemotherapy , the results are mixed. Some studies have found breast carcinoma patients treated with chemotherapy performed poorer than breast cancer patients not treated with chemotherapy[15-20] , whereas few studies did not [16].Debess. J.et al[26] conducted a study to assess cognitive function after surgery for early breast cancer but before initiation of adjuvant treatment.They performed a population-based study in the county of North Jutland, Denmark, including 124 women aged less than 60 years who had surgery for early breast cancer from 2004 - 2006. They were compared with an aged-matched group of 224 women without previous cancer selected randomly from the same population. The cognitive function of patients and controls was tested using a revised battery from the ISPOCD study. The neuropsychological tests did not reveal significant differences between patients and controls. Compared to the control group, breast cancer patients had a significantly 3-4 fold increased risk of experiencing cognitive impairment.Ahles. T. A.et al [19] have compared the neuropsychological functioning of breast cancer patients with invasive cancer and noninvasive cancer prior to adjuvant treatment. Breast cancer patients (N = 132) with invasive (Stages 1-3, N = 110, age = 54.1 +/- 8.1) or noninvasive (Stage 0, N =22,age=55.8+/-8.0) disease completed a battery of neuro psychological and psychological instruments following surgery but prior to initiation of chemotherapy, radiation or hormonal therapy. Matched healthy controls (N = 45, age = 52.9 +/- 10.0) completed the same battery of instruments. Data was collected from the patients regarding menstrual status, type of surgery, time of general anesthesia, CBC and platelets, nutritional status (B12 and folate),and thyroid function.Comparison of mean neuropsychological test scores revealed that all groups scored within the normal range; however, patients with Stage 1-3 cancer scored significantly lower than healthy controls on the Reaction Time domain ($p = 0.005$). Using a definition of lower than expected cognitive performance that corrected for misclassification error, Stage 1-3 patients were significantly ($p = 0.002$) more likely to be classified as having lower than expected overall cognitive performance (22%) as compared to Stage 0 patients (0%) and healthy controls (4%)

Conclusion

Assessment of cognitive functions in breast cancer patients has been studied which was attempted by very few studies. Standardized and validated tools were used in the study to assess various outcomes, makes the study findings more valid.Apart from the primary outcomes of interest, the study also documented the socio

demographic profile. The study showed poor performance in cognitive functions in breast cancer patients.

Limitations

1. The Sample size was not adequate to conduct sub group analysis / multivariate analysis of the data to rule out the role of confounding by various socio demographic variables.
2. This study is a cross sectional study. A longitudinal study would enable to determine stability of cognitive deficits.
3. All the domains of cognitive functioning and correlation with other neurobiological findings have not been assessed.

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