

A Clinical Study Of Behavioral Abnormality In Alzheimer's Dementia And Its Association With Severity Of Dementia

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Abstract:

Background: Dementia is a syndrome due to disease of the brain, usually of chronic origin and progressive nature along with disturbances of multiple higher cortical functions in clear consciousness. These include memory, thinking, orientation, comprehension, learning capacity, language and judgment. Alzheimer's disease typically begins with memory loss accompanied by later aphasia or other impairment in cognition and behavioral abnormality, in contrast, dementias that begin in frontal or sub cortical regions are less likely to begin with memory problems and more likely to have impairment in executive function or behavioral abnormalities. Prevalence of behavioral abnormality in Alzheimer's disease may increase from mild to severe forms, but some studies suggest a non-linear course with highest prevalence in intermediate course of the disease. A systematic review comprising of 59 studies showed hyperactivity, apathy showed high incidence and persistence, depression and anxiety showing moderate incidence and persistence while psychotic symptoms showed low incidence and persistence. Relation between severity of cognitive symptoms and behavioral abnormalities is yet to be clarified, while treatment of behavioral problems improve quality of life and reduces burden on caregiver. The present study will try to assess possible association between disease severity and behavioral abnormality and caregiver's burden.

Materials and Methods: It is a cross sectional study of 1 year duration to be done on 30 persons with Alzheimer's dementia diagnosed in LGBRIMH OPD as per ICD-10 fulfilling inclusion and exclusion criteria. Severity of dementia was assessed using dementia severity rating scale (DSRS) and behavioral abnormality was assessed using behavioral pathology of Alzheimer's dementia (BEHAVE -AD).

Results: Study population was comprised of both subjects of both gender with mean age 70.20 years (SD± 8.58 years). There were 11(36.7%) males and 19(63.3%) were females with their age varied from 56-79 years (Mean±SD 65.55±7.83) in case of male and 60-85 years (Mean±SD 72.89±7.97). Majority of them were married, among women majority were widows hailed from rural area (76.7%), belonged to extended family and 30% did not have any formal education. Majority (86.%) of our sample were Hindus followed by Muslims (6.7%). Majority of our subjects fall under the Middle socioeconomic status (46.7%) according to the Updated B G Prasad scale 2016. Average MMSE of the study population found to be 15.37(SD±2.94). In the present study behavioral symptoms were present in most of the patients (93.3%). In the present study diurnal rhythm disturbance was the most frequent symptom. Severity of dementia was significantly correlated with activity disturbances ($p=0.011$) and anxiety ($p=0.022$).

Conclusion: Most of the patients had at least one behavioral and psychological symptoms of dementia. Presence of behavioral symptoms have an adverse outcome on the disease process itself and also impacts caregiver's burden. Researches recently have focused on subtle behavioral symptoms called mild behavioral impairment(MBI) in cognitively normal adults that can predict cognitive decline. Further studies are needed in this area as it will help in early identification of person at risk for dementia and proper management plan for the person.

Key Word: Alzheimer's dementia, behavioral abnormality, behavioral and psychological symptoms of dementia(BPSD)

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I. Introduction

Dementia is a neurodegenerative disorder progressively effecting memory, thought and manifestations of behavioral symptoms. Neurodegenerative disorders are a heterogeneous group of disorders characterized by the progressive degeneration in both central and peripheral nervous system. The word dementia has been derived from a Latin word "dementatus," which means "out of one's mind."

Traditionally, different types of dementias are understood as irreversible and reversible dementia. The prototype of irreversible dementia is Alzheimer's dementia (AD). Despite the ever extending list of causes of

irreversible dementia, various clinic-based studies suggest that irreversible dementia account for 0–23% of all cases of dementia^{1,2,3}.

AD is characterized by insidious onset, progressive memory loss in the initial phase of the illness. Memory loss may be accompanied by or followed by disturbances in the other cognitive functions such as language, executive functions, and visuospatial functions (DSM-5). As the severity of the illness increases, cognitive disturbances may be accompanied by behavioral symptoms and in the most advanced stage patients require assistance for basic activities of daily living, i.e. bathing, toileting, and dressing, and patients may not be able to communicate, recognize their family members, and may become bed-bound.

Behavioral and psychological symptoms of dementia (BPSD) are common symptoms of the illness. Among them common symptoms which are manageable and unlikely to result in institutionalization are crying spells, lack of motivation, repetitive questioning etc. Symptoms that are moderately common but distressing for the caregivers are agitation, reduced sleep, inappropriate sexual behavior etc. Symptoms that are not common but are very distressing and also more likely to cause institutionalization are delusions, hallucinations, depression, behavioral symptoms like aggressiveness, restlessness and wandering behavior.

Early identification of AD is necessary, as it would help in planning early treatment and appropriate intervention. Research has shown that most people currently living with dementia have not received a formal diagnosis of the disorder. This “treatment gap” is applicable for India as well, with a study suggesting that 90% remain undiagnosed⁴.

II. Material And Methods

Site of Study: This was a cross sectional study conducted in LGB Regional Institute of Mental Health, Tezpur, a town in the North-Eastern part of India. This institute is a tertiary care institute providing mental health facility to the whole of North-East region.

Study population: Patients with diagnosis of Alzheimer's dementia according to ICD-10 attending outpatient department of LGBRIMH, Tezpur.

Study design: Design of the present study is descriptive design which follows the cross sectional way.

Sample size: The sample size consists of 30 subjects.

Duration of study: The duration of the study was for a period of one year from 01/06/2018 to 30/05/2019.

Sampling method: Purposive sampling technique employed. All the subjects that the investigator came across during the study period were selected after fulfillment of the various inclusion and exclusion criteria mentioned below.

Ethical consideration: The study was approved by ethical and scientific advisory committees of the institute. Before the start of the process all the individual who were selected for the study were explained about the subject matter of the study. After they were clear about this, consent was taken from them and they were also ensured that the information sought from them would be kept confidential.

Inclusion criteria:

1. Patients diagnosed as Alzheimer's dementia according to ICD-10 (newly diagnosed or follow up)
2. Including both gender
3. Informed consent

Exclusion criteria:

1. Those with other co-morbid psychiatric disorders
2. History of major medical or neurological disorder
3. History of any substance dependence except tobacco
4. Clinical examination, blood investigation or CT-scan suggestive of other neurological diseases

Tools for assessment:

1. Socio-demographic and clinical proforma
2. Mini Mental State Examination (MMSE)
3. Dementia severity Rating Scale (DSRS) for assessing severity of dementia
4. Behavioral pathology in Alzheimer's disease (BEHAVE-AD) rating scale

Procedure methodology:

After written informed consent was obtained, sociodemographic information was obtained using sociodemographic data-sheet. Details of illness were obtained using clinical data-sheet. From history, clinical examination and appropriate investigations wherever required were used to exclude other comorbidity or substance dependence except tobacco. Dementia severity was assessed using Dementia Severity Rating Scale (DSRS). Behavioral abnormality of the patient was assessed from the caregiver or observation during the

interview and if it is present it is assessed with Behavioral pathology in Alzheimer's Disease(BEHAVE-AD). Data acquired were recorded in a notebook.

Statistical analysis: Data acquired from the hospital based cross sectional study were initially recorded in the note book. These were master tabulated in MS EXCEL and then subjected to statistical analysis by IBM Statistical Package for the Social science (SPSS), version 20 and JMP 10 of SAS 9.3 software. Results of the study were presented by descriptive statistics such as frequency, percentage, mean, standard deviation (SD) and range.

Most of the Sociodemographic variables of the subjects were studied using descriptive statistics. Arithmetic mean and SD (mean ± SD) were frequently used for numerical variables. Frequency count and Chi square test were applied to assess Behavioral and Psychological Symptoms of Dementia(BPSD) assuming it as non parametric data. Since sample size of the study was 30, it was reasonable to use descriptive statistics and Analysis of Variance (ANOVA) variance ratio(F) test to assess severity of Alzheimer's dementia with respect to independent variables.

In order to ascertain association between BPSD and sociodemographic variables, logistic regression was used.

III. Result

There were 11(36.7%) males and 19(63.3%) females with their age varied from 56 to 79 years (Mean±SD=65.55±7.83) in case of male and 60-85 years (Mean±SD=72.89±7.97) in case of females.

Table 1: Frequency of Age and gender of sample

Age Group	Gender		Total
	Male	Female	
≤60 Yrs	4(36.4%)	1(5.3%)	5(16.7%)
61-70 Yrs	5(45.5%)	8(42.1%)	13(43.3%)
71-80 Yrs	2(18.2%)	6(31.6%)	8(26.7%)
> 80 Yrs	0(0%)	4(21.1%)	4(13.3%)
Total	11(36.7%)	19(63.3%)	30(100%)
Mean±SD (Yrs)	65.55±7.83	72.89±7.97	70.20±8.58
Range (Yrs)	56-79	60-85	56-85

Majority of them were married, among women majority were widows, most of the subjects hailed from rural area (76.7%), belonged to extended family and 30% did not have any formal education. Majority (86.7%) of our sample were Hindus followed by Muslims (6.7%). Majority of our subjects fall under the Middle socioeconomic status (46.7%) according to the Updated B G Prasad scale 2016.

Table 2 : Baseline Characteristics of Subjects

Variable	Sub Group	n(%)
Type of family	Nuclear	11(36.7%)
	Joint	6(20.0%)
	Extended	13(43.3%)
Domicile	Rural	23(76.7%)
	Urban	7(23.3%)
Religion	Hindu	26(86.7%)
	Muslim	2(6.7%)
	Others	2(6.7%)
Years of Formal Education	None	9(30.0%)
	1-5 Years	12(40.0%)
	6-10 Years	7(23.3%)
	11-15 Years	2(6.7%)
Occupation	Service	2(6.7%)
	Cultivation	4(13.3%)
	Business	5(16.7%)
	Home Maker	19(63.3%)
Marital Status	Married	29(96.7%)
	Unmarried	1(3.3%)
Socioeconomic Status	Upper Middle	6(20.0%)

Total Duration of illness(years) Mean± SD =2.60±1.63 Range (1-7) Yrs	Middle	14(46.7%)
	Lower Middle	7(23.3%)
	Lower	3(10.0%)
	1	8(26.7%)
	2	9(30.0%)
	3	8(26.7%)
	4	1(3.3%)
	5	2(6.7%)
7	2(6.7%)	
Total	30(100.0%)	

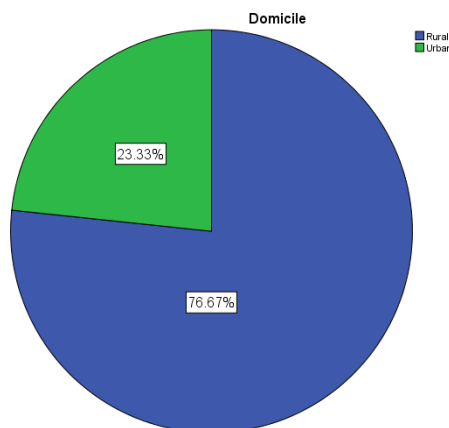


Fig 1: Pie diagram showing domicile of the sample

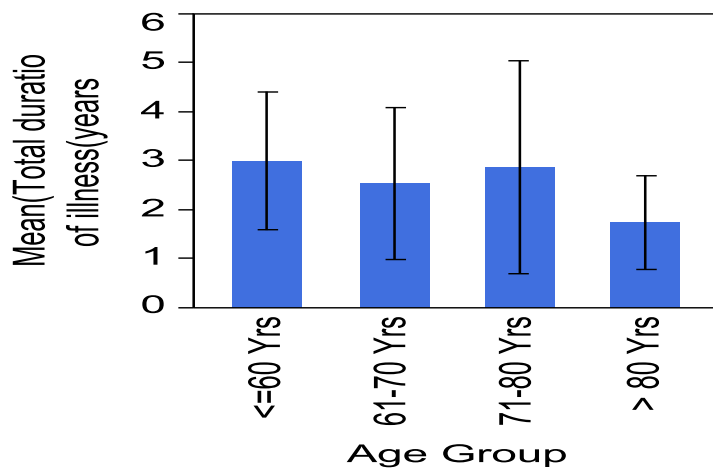


Fig 2: Error Bar chart showing age-wise mean total duration of subjects

Singh et al. Interpretation of MMSE(<21) found that 11 out of 11 male (100%) and 19 out of 19 female (100%) were increased odds of dementia

Range Interpretation of MMSE(<21) found that 11 out of 11 male(100%) and 19 out of 19 female (100%) were increased odds of dementia

Education Interpretation of MMSE(<21) found that 11 out of 11 male (100%) and 19 out of 19 female(100%) were abnormal for below 8th grade education.

Table 3: Mini-Mental State Examination(MMSE)

Sex	n	%	MMSE		p-Value
			Range	Mean± SD	
Male	11	36.7%	11-20	15.64±2.91	.709 ^{NS}
Female	19	63.3%	9-20	15.21±3.03	
Total	30	100.0%	9-20	15.37±2.94	

Assessment of severity of dementia using DSRS found that there were 8 patients (26.70%; 95% CI: 14.2-44.4%) were in mild category, 12 (40.00% ; 95% CI: 24.6-57.7%) in moderate category and 10 (33.30% ; 19.2-51.2% ; 95% CI: 19.2-51.2%) in severe category.

Table 4: Severity of dementia

DSRS Level	Frequency			Score	
	Count	%	95%CI	Range	Mean± SD
Mild	8	26.70%	14.2-44.4%	16-18	17.50±0.93
Moderate	12	40.00%	24.6-57.7%	19-36	25.50±6.39
Severe	10	33.30%	19.2-51.2%	37-51	44.10±5.07
Total	30	100.00%		16-51	29.57±11.98

Behavioral abnormality i.e. Behavioral and psychological symptoms (BPSD)of Alzheimer's dementia using BEHAVE-AD scale found that there were 3(10.00%) severe cases in case of anxiety and 1(3.33%) case of Hallucinations in severe category. In moderatecategory, 7(23.33%) cases were with Paranoid symptoms followed by 6(20.00%) in Aggressiveness.

Table 5: Behavioral and psychological symptoms (BPSD) of Alzheimer's dementia

Count,(%)	Not Present	Mid	Moderate	Severe
Paranoid symptoms	18(60.00%)	5(16.67%)	7(23.33%)	0(0.00%)
Hallucinations	17(56.67%)	9(30.00%)	3(10.00%)	1(3.33%)
Activity disturbances	12(40.00%)	14(46.67%)	4(13.33%)	0(0.00%)
Aggressiveness	15(50.00%)	9(30.00%)	6(20.00%)	0(0.00%)
Diurnal rhythm disturbances	10(33.33%)	15(50.00%)	5(16.67%)	0(0.00%)
Affective disturbances	26(86.67%)	3(10.00%)	1(3.33%)	0(0.00%)
Anxiety	14(46.67%)	9(30.00%)	4(13.33%)	3(10.00%)

In mild category, there were 15(50.00%) cases were Diurnal rhythm disturbances followed by 14(46.67%) cases with Activity disturbances and 9(30.00%) cases each in Hallucinations and Anxiety. A maximum of 26(86.67%) cases were found Affective disturbances in not present category followed by 18(60.00%) with Paranoid symptoms. Thus most frequent behavioral symptom is diurnal rhythm disturbances (67.67%) followed by activity disturbances (60%).

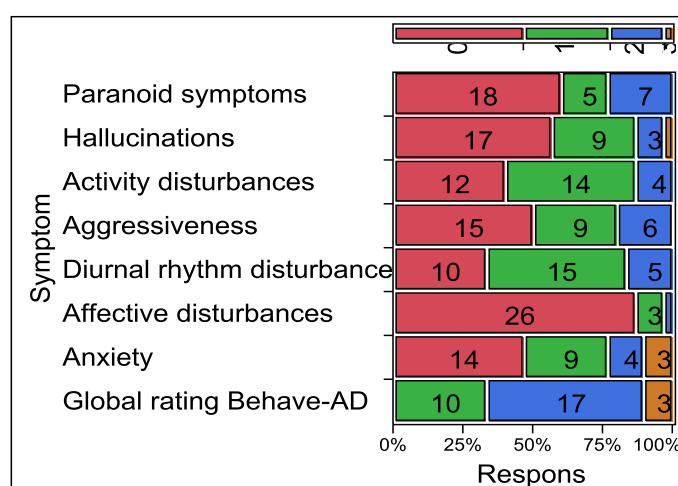


Fig 3 : Behavioral and psychological symptoms (BPSD) of Alzheimer's dementia

Association between dementia severity and BPSD found that DSRS was significantly correlated with activity disturbances ($p=0.011$) and anxiety ($p=0.022$), while it was found to be insignificant in case of Paranoid symptoms, Hallucinations , Aggressiveness, Diurnal rhythm disturbances, Affective disturbances, and Global rating Behave-AD.

Table 6: DSRS and BPSD association

Symptoms	Mean±SD	F	d.f.	p-value
Paranoid symptoms				
Not Present	31.06±12.72	0.36	2,27	0.698 ^{NS}
Mild	28.40±10.92			
Moderate	26.57±11.72			
Hallucinations				
Not Present	29.76±12.46	1.25	3,26	0.313 ^{NS}
Mild	25.11±9.93			
Moderate	38.00±13.53			
Severe	41.00			
Activity disturbances				
Not Present	21.92±7.09	5.29	2,27	0.011*
Mild	34.50±12.59			
Moderate	35.25±11.21			
Aggressiveness				
Not Present	28.00±11.64	0.29	2,27	0.753 ^{NS}
Mild	31.89±11.93			
Moderate	30.00±14.42			
Diurnal rhythm disturbances				
Not Present	28.50±12.09	0.3	2,27	0.745 ^{NS}
Mild	29.00±12.21			
Moderate	33.40±12.93			
Affective disturbances				
Not Present	30.27±12.51	0.55	2,27	0.586 ^{NS}
Mild	27.33±6.66			
Moderate	18.0			
Anxiety				
Not Present	33.00±12.78	3.78	3,26	0.022*
Mild	21.11±7.61			
Moderate	27.50±9.88			
Severe	41.67±3.06			
Global rating Behave-AD				
Mild	28.00±13.17	0.17	2,27	0.846 ^{NS}
Moderate	30.71±11.99			
Severe	28.33±11.15			
Total	29.57±11.98			

Study of association of BPSD with various socio-demographic variables found insignificant linkage between Behavioral abnormality and patients' socio-demographic characters such as Age Group , ($p=0.182$), gender, ($p=0.624$), Type of family, ($p=0.145$), No of family members, ($p=0.673$), Domicile , ($p=0.197$), Religion, ($p=0.683$), Years of formal education, ($p=0.586$), Occupation, ($p=0.316$), Marital status, ($p=0.999$), Socioeconomic status, ($p=0.873$) and Total duration of illness years, ($p=0.616$).

Table 7: Logistic Regression of BPSD with various socio-demographic variables

Socio-demographic Variable(s)	B	S.E.	Wald Chi Sq (1 df)	p-value	Exp(B)	95% C.I.for EXP(B)	
						Lower	Upper
Age Group	-1.35	1.01	1.78	0.182	0.26	0.04	1.88
Sex	1.46	2.98	0.24	0.624	4.31	0.01	1473.89
Type of family	-1.31	0.90	2.13	0.145	0.27	0.05	1.57

No of family members	-0.11	0.26	0.18	0.673	0.90	0.54	1.50
Domicile	-2.87	2.22	1.67	0.197	0.06	0.00	4.42
Religion	-0.40	0.98	0.17	0.683	0.67	0.10	4.59
Years of formal education	0.79	1.45	0.30	0.586	2.20	0.13	37.98
Occupation	0.82	0.82	1.00	0.316	2.28	0.46	11.37
Marital Status	15.29	40192.91	0.00	0.999	4.37E+06		
Socioeconomic status	0.17	1.06	0.03	0.873	1.19	0.15	9.48
Total duration of illness years	-0.17	0.35	0.25	0.616	0.84	0.42	1.66
Constant	-11.71	40192.91	0.00	1.000	0.000		

IV. Discussion

The mean age of the study population was 70.20 (SD±8.58) years. This is comparable to a previous study of Park S et al in which mean age was 72.9 years⁶. There were 11(36.7%) males and 19(63.3) females with mean age of 65.55±7.83 years in case of male and 72.89±7.97 years in females, similar to the result of a study in which males had accounted for 37.8% of the patients⁶.

Majority of the subjects in the study are from rural area, 23 subjects (76.7%) are from rural area. It is similar to data from census, 2011 in which 71% of the elderly live in rural India. In all the states, except two states, Goa and Mizoram, a higher proportion of the elderly lives in rural areas than in urban areas⁷.

The study sample has more subjects belonging to extended family (43.3%) than nuclear (36.7%) and joint (20.0%) families. This seems contrary to the latest Census of India (2011) data that depicts nuclear family to form the majority of Indian households (70%), but it can be explained by the age group of this study population where extended family is quite common.

In our study, socioeconomic status was assessed using Updated B G Prasad scale 2016. As per this scale, majority of our cases fall under the middle socioeconomic status (46.7%) followed by lower middle (23.3%), lower (10%) and upper middle (6%) socioeconomic status⁸.

Of the study sample, 30% were illiterate, 40% had at least 5 years of formal education, 23.3% had 11-15 years of education and only 2% had more than 15 years of formal education. Literacy rate of India as per last census was 74.04%⁷. High illiteracy rate in the study sample may be explained by the age group of the target population.

Almost 2/3rd (63.3%) of the study sample are homemakers, 16.7% involved in business, 13.3% are into cultivation and 6.7% are in the service. Although subjects were in the cultivation or business, when the symptoms became severe they are no longer being able to continue the work. Also people involved in the service had to take or apply for voluntary retirement after their symptoms became incompatible for the service. High percentage of homemakers is explained by high number of female in the study sample.

Majority (86.6%) of our sample were Hindus followed by Muslims (6.7%) and others consisting of Buddhism and Christianity (6.7%). A preponderance of Hinduism can be matched with the latest Census 2011 data of the region (61.47% Hindus, 34.22% Muslims, 3.74% Christians).

Mean duration of illness in the study sample was 2.60(SD±1.63) years in the range of 1 to 7 years. The duration of dementia did not show any variation in the behavioral symptom profile and also on the severity of illness. Also as the present study is a cross sectional study it is not possible to comment on the evolution and progression of the symptoms.

The average MMSE of the study population found to be 15.37(SD±2.94). Average MMSE score in three studies on Alzheimer's dementia patients were 20.09 by Park S et al is comparable to the result of the present study⁶. Gender-wise analysis of MMSE revealed male having insignificantly higher odd of MMSE than female. In an elderly community-based sample, Ganguli et al. reported a small but significant difference favoring women on the MMSE, while Fillenbaum et al. in a different elderly community-based sample, found a small difference favoring men⁹. O'Conner et al reported no gender difference on total MMSE score in a large sample of patients aged 75 years or older from a general practice¹⁰. Buckwalter et al. (1993) found that MMSE performance may differ between men and women with AD and that differences might pertain only to discrete areas of cognitive functioning¹¹.

Assessment of severity of dementia using DSRS found that 26.70% in mild category, 40.00% in moderate category and 33.30% in severe category. More number of subjects in the mild category may be due to increased awareness of the illness among people.

In the present study behavioral symptoms were present in most of the patients (93.3%). Study by Lyketssos et al found that more than 80% of patients with dementia shown to have at least one neuropsychiatric symptoms¹².

Published data on the prevalence rates of NPS in AD patients varies widely. This may be due to heterogeneity in the study setting, population demographics, evaluation methods or severity of cognitive impairment^{13,15}.

In the present study diurnal rhythm disturbance was the most frequent symptom with its presence in 2/3rd (66.67%) of subjects, followed by activity disturbances (60%). In diurnal rhythm disturbance most had the complaint of repetitive awakening at night, only two subjects had reduction in sleep cycle to 50-75% than earlier.

In a study by Rongve et al. reported sleep disturbance in 64% of participants diagnosed a Alzheimer's dementia¹⁴. Persons living with Alzheimer's disease (AD) have disrupted sleep, with prevalence rates as high as 71%¹⁶.

Activity disturbances are the second (60%) most common behavioral disturbance in the current study. In activity disturbances the most common type was wandering behavior, followed by purposeless activity and inappropriate activity. A study by Barrett B et al reported a prevalence of wandering behavior in roughly one-quarter of participants (26.1%) by their caregivers at one or more time point, across all study visits. In the present study there was no significant association between various social-demographic variables and behavioral and psychological symptoms of Alzheimer's dementia (BPSD). This may be due to small sample size in the study.

Severity of dementia was significantly correlated with activity disturbances ($p=0.011$) and anxiety ($p=0.022$), while it was insignificant in case of paranoid symptoms, hallucinations, aggressiveness, diurnal rhythm disturbances, affective disturbances and global rating score of Behave-AD. This is comparable to previous study by Teri et al. in which anxiety was significantly related to level of cognitive impairment. Subjects with more severe cognitive impairment were more likely to be anxious than those with mild to moderate cognitive impairment¹⁵. Also in a study by Yang et al. assessing Neuropsychological characteristics of wandering behavior in Patients with drug-naive Alzheimer's Disease found AD patients with wandering have disproportionately high cognitive deficit¹⁸.

V. Conclusion

The study was conducted with the aim to assess non cognitive behavioral symptoms in Alzheimer's dementia. Presence of behavioral symptoms have an adverse outcome on the disease process itself and also impacts caregiver's burden. Assessing dementia severity and behavioral symptoms it was found that severity of dementia was significantly correlated with activity disturbance and anxiety.

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