A Non Randomized Case Control Study on Prevalence of Cognitive Deficits in Patients undergoing de-addiction therapy for Alcohol use Disorder in General Hospital Psychiatry Unit in North India

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ABSTRACT

Introduction: The Alcohol abuse known to cause cognitive impairments in human beings ranging from mild reversible conditions to debilitating neurological conditions like korsakoff Syndrome and Alcohol- Induced Persisting Dementia. The etiological process of cognitive deficits is complex with influences from genetic loading, nutritional status and duration of alcohol abuse. Both prefrontal cortex and medial temporal lobe are most vulnerable parts of brain to be affected by ethanol. The underlying mechanisms involved in cognitive disturbances were structural damages, neurotoxicity and circuitry degradation.

Material and Methods: This Study was conducted in General hospital Psychiatry Unit from 01Jul 2020 to 31Dec Dec 2020 after obtaining ethics committee approval. By Convenient Method Sample size of 79 consecutive patients admitted for de-addiction therapy for alcohol use disorder and 79 healthy male were enrolled as cases and control respectively after taking informed consent.

Results: Statistical analysis was performed by using SPSS-version-20. The Pearson Chi Square test and Student t-test were performed for comparison of quantitative variables with 5% probability level was considered as statistically significant i.e., P value <0.05. Memory Scale subtests revealed 30% deficits in cases versus 16% control with P value < 0.001. Total Score on Memory Scale were 9.3797 and 2.3544 in cases and control respectively with P value <0.001. Cognitive deficits noted on Memory scale subset among cases were 29.85% - Attention & Concentration,9.5%- Recent Memory, 5.7%- Remote Memory 31.7% - Immediate Recall, 21.5%- Delayed Recall, 19% - Retention of Similar pairs, 21.5% -Retention of Dissimilar Pairs, 16.5% - Visual Retention and 10.5%- Recognition.

Conclusions: Memory Scale subtests on immediate memory, recent memory, working memory and recognition revealed 30% deficits in cases versus 16% control with P value < 0.001

Keywords: Alcohol use Disorder, Cognitive Deficits, De-Addiction, Postgraduate Institute of Memory Scale, Neuropsychological Test

INTRODUCTION

Alcohol is an organic solvent known for its relaxing and intoxicating effects in human beings since antiquity. Various alcohol based beverages are beer, spirit (vodka, whisky, rum, gin) and wine.[1] Alcohol use disorder accounts for 5.1 % of disability-adjusted life years (DALY'S) worldwide.[2] The disability in alcohol use disorders results due to various neuropsychiatric conditions and bodily injuries.[3]

Previous studies have reported up to 70% cognitive deficit in alcoholic subject on various memory domains like attention, concentration, visual-motor coordination, cognitive flexibility, problem solving, reasoning, perception, and information processing speed.[4] Notwithstanding there is a considerable gap in knowledge and paucity of research in Asian Countries with regard to prevalence, extent and pattern of neurocognitive deficit burden among alcoholic patient. Therefore, current study was undertaken to find out cognitive deficits by using Post graduate institute of Memory Scale (PGI-MS) Neuropsychological tool standardized on Indian population with validity as correlation of 0.71 with Boston Memory Scale and 0.85 with Wechsler Memory scale.

The various mechanism of cognitive deficits in alcoholics patients are due to direct effects of alcohol on gamma-amino butyric acid (GABA) receptors & N-methyl-D-aspartic acid (NMDA) receptors.[5] The low doses of alcohol enhances influx of chloride into the neurons whereas when high doses of alcohol is consumed repeatedly, it downgrades GABA receptor subunits.[6] Chronic alcohol intake activates inflammatory mediators through glial cells intracellular signaling pathways to generate cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), the pro inflammatory cytokines IL-1b, TNF-, up regulation of COX-2 (cyclooxygenase-2) and iNOS (inducible nitric oxide synthase) levels.[7]

MATERIAL AND METHODS

This case control study was carried out in a tertiary care hospital with psychiatric inpatient facility in Uttar Pradesh

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- India from 01Jul2020- 31Dec2020.
Freshly diagnosed cases of alcohol dependence syndrome (ADS) after fulfilling inclusion and exclusion criterion.

Sampling technique and sample size: A non-probability sampling technique of convenience sampling method was employed (where samples are selected from population randomly because they were conveniently available to researchers. This study has been conducted as independent cases and controls with 1 control(s) per case. Prior data indicate that the probability of exposure among cases is 7%[8], hence we needed minimum 64 case patients and 64 controls to be able to reject the null hypothesis that the exposure rates for case and controls are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. Hence based on the prevalence of alcohol dependence syndrome, a total of 80 case and 80 control patients (statistically calculated) in a tertiary care hospital, Bareilly UP from 01Jul 2020 to 31 Dec2020 were enrolled in this study.

Ethical Consideration
Necessary ethical approval was obtained from the institutional ethics committee. The participants signed informed consent form after they were given a full explanation about the purpose of the study, assurance about the confidentiality of the information and that the participation was voluntary.

Inclusion criteria for cases: 20-59yrs male, freshly diagnosed cases of ADS as per ICD-10, education level as middle standard to graduate

Exclusion criteria for cases: Case with relapses or failed to turn up for subsequent reviews.

Inclusion criteria for control: (a) 20-59 yrs. healthy males with educational qualification middle standard to graduation (b) Nondependent pattern alcohol user/teetotaler.

Exclusion criteria for both groups (a) Other psychoactive substance use disorder. (b) Co-morbid psychiatric, medical or neurological disorder (c) Regular use of any medication known to alter cognitive function.

Study design: Patients admitted with clinical features of Alcohol dependence Syndrome as per ICD-10 criteria underwent evaluation for severity of alcohol abuse by alcohol use disorder identification test (AUDIT), CAGE questionnaire and structured Clinical interview by psychiatrist. All cases and control underwent Neuropsychological test of Post Graduate Institute- of Memory Scale (PGI-MS) by Clinical Psychologist. In sample size of 80 cases, one case was dropped in the beginning of study.
All cases of alcohol use disorder (AUD) underwent reassessment at 24 weeks Neuropsychological tool of PGI-Memory Scale.

Instrument: Post graduate Memory scale (PGI-MS), a neuropsychological subset of ten tests with:
(a) Language: English and Hindi
(b) Levels: Above the age of 20 yrs.

(c) Reliability: The test- retest reliability ranged between 0.70 and 0.84 for organic psychotic disorder, 0.48 and 0.84 for neurotic normal group.
(d) Validity: PGI Memory Scale was found to have correlation of 0.71 with Boston Memory Scale and 0.85 with Wechsler Memory scale. The test was compared with well-known scales like Bhatia scale and WAIS.

STATISTICAL ANALYSIS
The statistical analysis was performed by using SPSS version 20.The clinical profile of patients was analyzed by chi-square test for qualitative variables. Student t test was performed for comparison of quantitative variables. 5% probability level was considered as statistically significant i.e., p <0.05.

RESULTS
All the statistical analyses were performed using SPSS version 20.The clinical profile of patients was analyzed by Pearson Chi-square test for qualitative variables. Student t test was performed for comparison of quantitative variables. 5% probability level was considered as statistically significant i.e., p< 0.05.
The demographic data distribution in study groups illustrated at Figure 1A, shows all cases and controls were male gender. Among study group 36.7% cases (n=58) versus and 43.6% (n=69) were < 30 years of age. The mean score on alcohol screening tool of Alcohol Use Disorder Identification Test (AUDIT) among cases and controls were 13.03 and 6.10 respectively with statistically significant p value < 0.001.The mean duration of alcohol abuse in cases was 12 years versus 9 years in control. In study group 35% cases (n=71) versus 39.9% (n=63) control subjects were 10th educated where as 1.3%cases (n=2) &4.4% (n=7) were graduate and above educated. In study group 60.8% (n=48) cases versus 1.3% (n=1) control were abusing >40gm of ethanol /day.
The Cognitive deficits that are recorded as dysfunction rating score severity N, 2 & 3 on PGI-Memory Scale subtest as below
- Attention and Concentration scale revealed deficits on Dysfunction rating score severity 2&3 in cases were - 29.8% (n=47) versus 13.9 %(-n=22) in Controls with P value <0.001. Among study groups in 20.3% cases (n=32) and 36.1% (n=57) revealed nil dysfunction rating score as normal. (Fig 1B; Table 2A)
-Recent Memory Scale revealed deficits on Dysfunction rating score severity 2&3 were-9.5% in cases (n=15) versus nil in controls (n=0) with P value <0.001. Among study group 40.5% cases (n=64) and 50% control (n=79) reveals no cognitive deficits with dysfunction rating Score as normal. (Fig 1B)
- Remote Memory Scale revealed deficits on Dysfunction rating score severity 2&3 were- 5.7% (n=9) in cases versus 0.6% (n=1) in controls with P value <0.001. Among study group 43.3% cases (n=70) and 49.4% control (n=78) reveal nil cognitive deficits with dysfunction rating Score as normal. (Fig 1B)
-Immediate Recall scale revealed deficits on Dysfunction
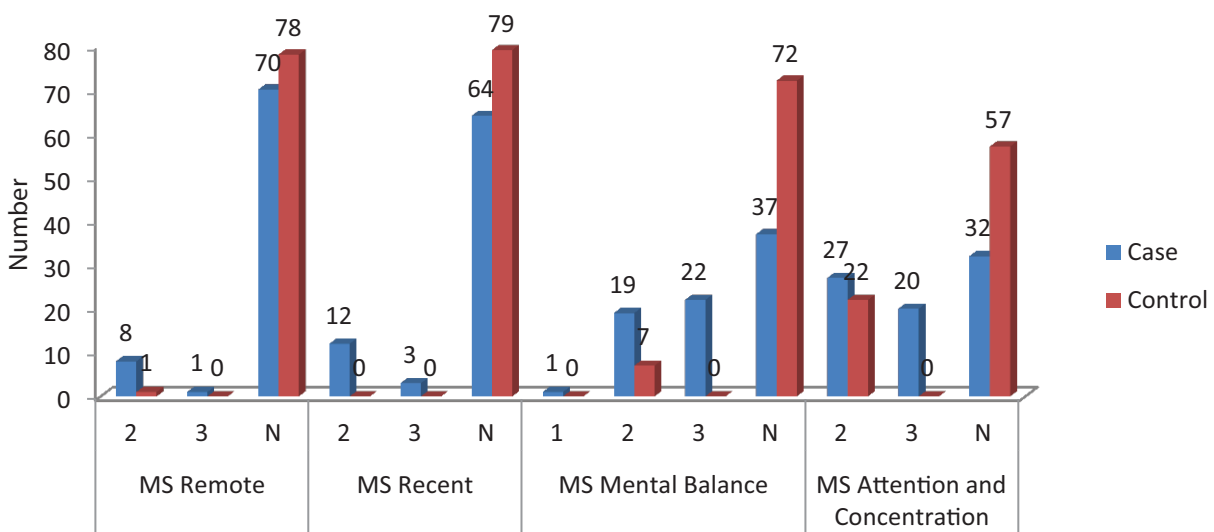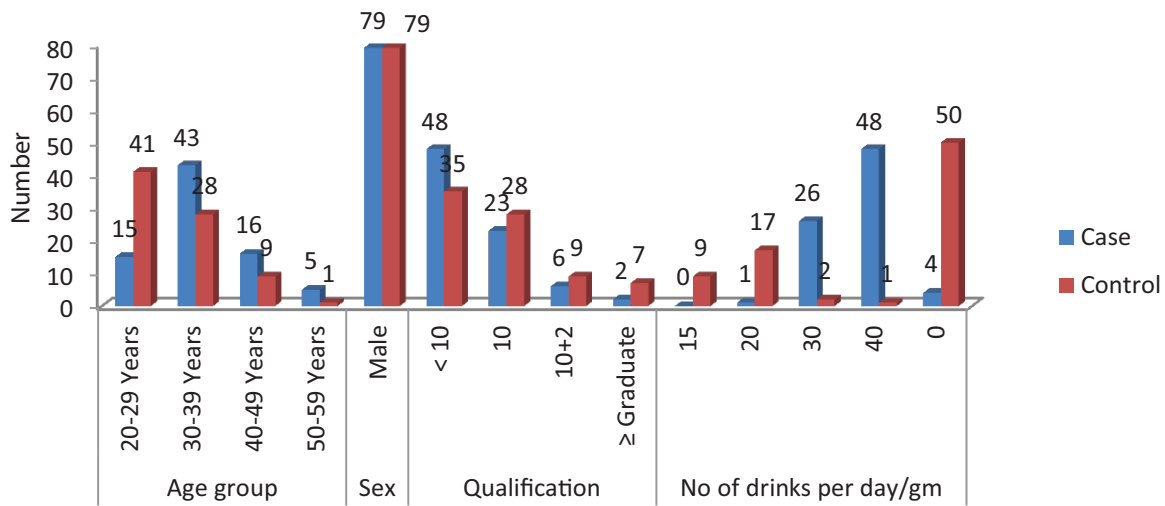
MS= Memory Scale; 2- Dysfunction rating Score Severity; 3- Dysfunction Score Severity; N- Normal (No cognitive deficits)
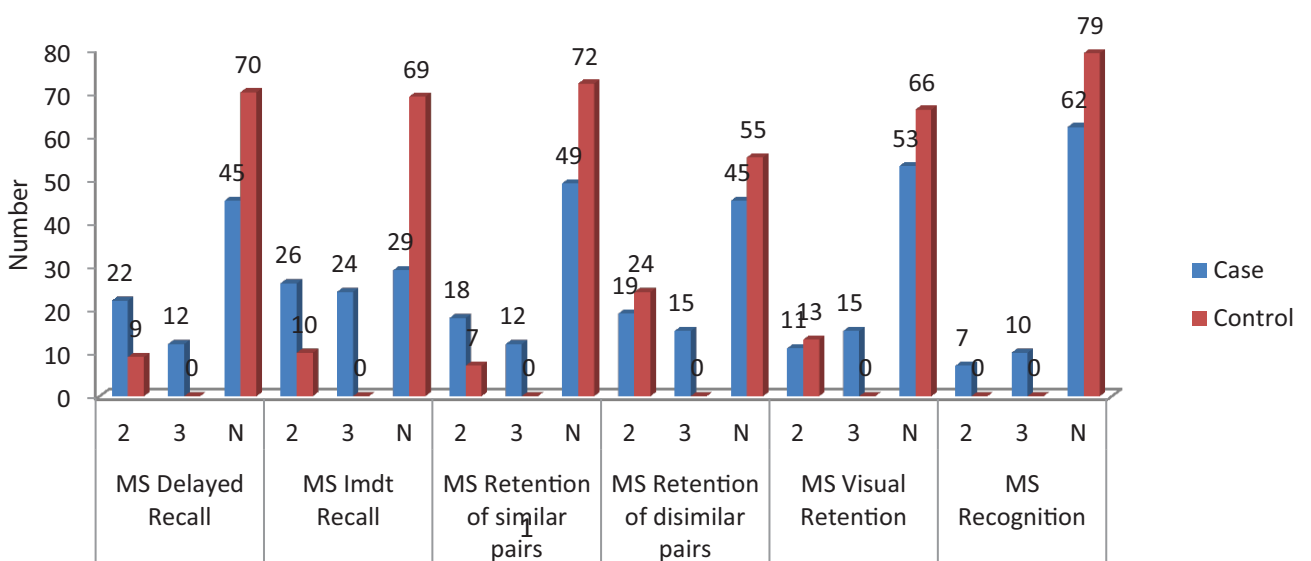
MS= Memory Scale; 2- Dysfunction rating Score Severity; 3- Dysfunction Score Severity; N- Normal (No cognitive deficits)

Figure-1A: Distribution of demographic data in the study group; Figure-1B: Frequency distribution of different parameters in the study group; Figure-1C: Frequency distribution of different parameters in the study group

Dysfunction Rating Score (DRS)			Group		Total	P-value
			Case	Control		
Attention and Concentration	2	Count	27	22	49	<0.001
		% of Total	17.1%	13.9%	31.0%	
	3	Count	20	0	20	
		% of Total	12.7%	0.0%	12.7%	
	N	Count	32	57	89	
		% of Total	20.3%	36.1%	56.3%	
Total		Count	79	79	158	
		% of Total	50.0%	50.0%	100.0%	
2 - Dysfunction rating Score Severity; 3 - Dysfunction Score Severity; N- Normal (No cognitive deficits)						
Table-2: A PGI- Memory Scale – Attention and Concentration						

rating score severity 2&3 in cases were – 31.7% (n=50) in cases versus 6.3 %(n=10) in Controls with P value <0.001. Among Study groups 18.4% cases (n-29) & 43.7% control (n=69) revealed nil cognitive deficits with Dysfunction Rating Score as normal. (Fig 1C)

- Delayed Recall scale revealed deficits on Dysfunction rating score severity 2&3 in cases were – 21.5% (n=34) versus 5.7 %(n=9) in Controls with P value <0.001. Among Study groups 28.5% cases (n-45) & 44.3% control (n=70) reveals nil cognitive deficits with dysfunction rating score as normal. (Fig 1C)

- Mental Balance Scale revealed deficits on Dysfunction rating score severity 2&3 in cases were-12.6 % (n=20) versus 4.4% (n=7) in controls. Among study groups about 23.4% (n=37) and 45.6% control (n=72) revealed nil cognitive deficits with dysfunction rating score as normal. (Fig 1B)

- Retention of Similar Pairs Scale revealed deficits on Dysfunction rating score severity 2&3 in cases were – 19% (n=30) versus 4.4 %(n=7) in Controls with P value <0.001. Among Study groups 31% cases (n-49) & 45.6% control (n=72) revealed nil cognitive deficits with dysfunction rating score normal. (Fig 1C)

- Retention of Dissimilar Pairs Scale revealed deficits on Dysfunction rating score severity 2&3 in cases were – 28.5% (n=45) versus 34.8 %(n=55) in Controls with P value <0.001. Among Study groups 28.5% cases (n-45) & 34.8% control (n=55 revealed nil cognitive deficits with dysfunction rating score as normal. (Fig 1C)

- Visual Retention Scale revealed deficits on Dysfunction rating score severity 2&3 in cases were – 16.5% (n=26) versus 8.2 %(n=13) in Controls with P value <0.001. Among Study groups 33.5% cases (n-45) & 41.8% control (n=66) revealed nil cognitive deficits with dysfunction rating as score normal. (Fig 1C)

- Recognition Scale revealed deficits on Dysfunction rating score severity 2&3 in cases were – 10.7% (n=17) versus nil n=0) in Controls with P value <0.001. Among Study groups 39.2% cases (n-62) & 50% control (n=79) revealed nil cognitive deficits with dysfunction rating score normal. (Fig 1C)

DISCUSSION

Earlier studies findings shows variable degree of cognitive deficits in alcoholics patients tested on various neuropsychological tools for memory, intelligence and learning with focus on cognitive functions like decision making, self-regulations, and forethought and impulse control. In our study prevalence of cognitive deficits in cases were up to 32% versus 15% in control group. In our study the total dysfunction score on PGI- Memory Scale noted to be 9.3797 in cases versus 2.3544 in controls. During follow up at 24 weeks, there was remarkable improvement in cognitive decline among all cases of alcohol spanning across all ten subsets of PGI-Memory scales. The residual deficits of PGI- memory scale at 24 wks recorded were 5% in recent memory,7% in attention & concentration , 9% in delayed recall ,8% in Immediate memory, 11% in retention of similar pairs, 10% in retention of dissimilar pairs, 9% in visual retention and 11% in retention of similar pairs. In a similar study Smeraldi, Movalli et al have reported up to 72% cognitive deficits in alcoholics among which 45.7% had generalized declined in cognitive functions, 26.1% had deficits in verbal memory and 32.6% demonstrated deficits in working memory. In one similar study testing by FAB, wherein majority of alcoholic subjects showed lower scores as compared to non-alcoholic controls with P Value <0.0001).[9] Conceptualization difference was found in Type IV alcoholics with mean scores (P <0.01) as compared to the non-alcoholic controls and other subgroups of alcoholics. Mental flexibility between alcoholics and non-alcoholics was not statistically significant between non-alcoholic control and the subgroups of alcoholics P <0.0001), motor programming was significantly lower (P<0.001) in alcoholic patients as compared to non-alcoholic controls. Inhibitory Control subset was also significantly lower (P< 0.01) in alcoholic patients as compared to non-alcoholic controls with P=0.0003. The studies show most problem drinkers had mild neuropsychological difficulties, which improve within a year of abstinence.[10] Study by Saraswat et al. 2006[11] where in 30 alcohol dependent patents 15 controls Trail making test, stroop test revealed that patient group performed poorly in all the tests. Duration of abstinence over past one year correlated with performance on Stroop test. The majority of alcoholic subjects showed lower scores as compared to non-alcoholic controls in Autobiographical memory test (AMT) study on 26 nondependent drinkers compared with 26 detoxified individual Philip & William (1997), Stock well et al (1974) found notable difference in cognitive variable

with higher score in brain dysfunction inventory (BDI) among dependent drinker than nondependent drinker with P value < 0.001. The early studies hypothesized Fluency, abstract reasoning, cognitive flexibility and psychomotor speed proved (Rt) hemisphere (nonverbal) function measured by test on ROCF (Rey Osterrieth complex figure test were more frequently effected than (Lt) hemisphere verbal memory measured on psychological instruments by Hopkins verbal learning test (Benedict et al 1998). In a similar study the functional changes have been reported in humans after adolescent alcohol use compared to light or non-drinking adolescents, as evidenced by differences in fMRI BOLD-responses during learning and memory tasks and on a cue reactivity task.[12] Hippocampus ERPs have been found in adult rats after binge-like alcohol exposure during adolescence. Structural and functional changes may underlie impairments in neurocognitive performance.[13] The early alcohol use in humans is likely to be a risk factor for later alcohol abuse and alcohol addiction. Fluency figural test the no of unique design reproduced correctly in previous studies shown significant impairment in drinker compare to control with P value < 0.001).

In similar studies in 2004 by Zinn (27 subject with alcohol use disorder (AUD),18 control)[14] and by scheurich with (57 subjects with alcohol use disorder, 59 control) noted on neuropsychological measures with WAIS III (Wechsler adult intelligence scale III) , WAIS-R(Wechsler adult intelligence scale, LPS IQ (Leistungs- prufsystem, Horn) a German test) finding consistent with AUD<control in Verbal memory and vocabulary.[15] During abstinence alcohol cases have shown remarkable improvement in cognitive deficits which is explainable by process of neuro-adaptibility, neurogenesis sets in after noxious insult to brain parenchyma withdrawn.

Study Limitations

To generalize prevalence of Cognitive deficits finding globally a cohort study of large sample size would be required. Individual's variation in intellectual functioning coupled with difference in their education level might have been confounding factors by PGI- Memory Scale test.

CONCLUSION

In comparison to healthy control, in about 32% AUD cases cognitive deficits were recorded across subset tests of PGI-MS. The cognitive deficits recorded in the form of Dysfunction Rating Score of variable severity ranged from 4% to 32% in Alcohol Cases in all ten subsets of PGI-Memory Scale ranging from attention and concentration, remote memory, recent memory, mental balance, immediate recall, verbal retention of similar and dissimilar pairs, visual retention and recognition. During abstinence period all cases of alcohol showed remarkable (approx. 70%) improvement in dysfunction rating score measured by PGI-MS sub test. To extrapolate findings of neuropsychological tool score into real life task like learning from past experiences, self-regulation, and impulse control a cohort study with real life tasks as determinant of cognitive function needs to be incorporated. Intact cognitive functions play a role in persistence /self-regulation, forethought and impulse control necessary for adherence with treatment for relapse prevention strategies in alcoholic patients.

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