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Relationship between Cognitive Impairment and Socio-Demographic and Clinical Variables in COPD and Bronchial Asthma: A Comparative Study

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Abstract: *This is a cross sectional comparative case control study assessing the Relationship between cognitive impairment and socio demographic and clinical variables in chronic obstructive pulmonary disease (COPD) and Bronchial Asthma in comparison to healthy individuals. It is found that patients with COPD have significant cognitive deficits in comparison to patients with bronchial asthma.The cognitive impairment is related to to age , educationa ,occupation ,duration , severity of illness and steroid medication.*

Keywords*: cognitive impairment, COPD, Bronchial Asthma, socio demographic, clinical variables*

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I. Introduction

Cognitive dysfunction is associated with increased mortality and disability; however, it remains poorly understood in COPD. One review examined mechanisms of injury and dysfunction to the brain and considers the methods used to evaluate cognition, and assembles evidence concerning the nature and level of cognitive impairment in COPD. Main findings of this review were: 1) there may be a pattern of cognitive dysfunction specific to COPD; 2) cognitive function is only mildly impaired in patients without hypoxaemia; 3) the incidence of cognitive dysfunction is higher in hypoxaemia; 4) hypoxaemia, hypercapnia, smoking and comorbidities (such as vascular disease) are unlikely to account for all of the cognitive dysfunction seen in COPD; 5) there is weak or no association between cognitive function and mood, fatigue or health status; 6) cognitive dysfunction may be associated with increased mortality and disability; and 7) there is limited evidence for a significant effect of treatment on cognitive function.[1]

Three groups of patients with COPD whose hypoxemia was mild (N = 86), moderate (N =155), or severe (N = 61) were compared with age- and education-matched nonpatients (N = 99). The rate of neuropsychologic deficit rose from 27% in mild hypoxemia to 61% in severe hypoxemia. Various neuropsychologic abilities declined at different rates, suggesting differential vulnerability of neuropsychologic functions to progress of COPD. Multivariate analyses revealed a consistent significant relationship between degree of hypoxemia and neuropsychologic impairment, but the amount of shared variance was small (7%). Increasing age and lower education were also associated with impairment.[2]

Eighteen patients with chronic obstructive pulmonary disease (COPD) were administered a series of pulmonary, neurological, and neuropsychological measures to test if there was an effect of COPD on neurological and cognitive functioning. Overall, there was no evidence of general dementia in this sample. Measures of immediate and delayed memory, complex attention, and speed of information processing correlated highly with arterial carbon dioxide partial pressure and, to a lesser extent, with oxygen partial pressure. Measures of language abilities, perceptual-motor functioning, and simple attention generally were not related to arterial gas pressures. A similar pattern of findings was obtained when group differences were examined between participants classified as severely hypoxic or mildly hypoxic, although group differences were mitigated by premorbid IQ differences. And it was concluded that hypoxia in COPD results in a relatively focused pattern of impairment in measures of memory function and tasks requiring attention allocation. The memory dysfunction may be related to involvement of

limbic memory regions necessary for explicit memory. The attentional deficits were attributed to diffuse brain involvement resulting in reduced resource allocation. Early diagnosis and treatment of the hypoxia is essential.[3]

A study done by Inclazi et al to identify predictors of cognitive decline in patients with hypoxemic COPD on continuous oxygen therapy. And it was found that cognitive decline is faster in the presence of severe bronchial obstruction and parallels the worsening of the affective status in COPD patients on oxygen therapy.

The onset of depression rather than baseline depressive symptoms seems to be a risk factor for cognitive decline.[4] Study done by Kozora et al to examine neuropsychologic functions in patients with chronic obstructive pulmonary disease and mild hypoxemia compared with patients with mild Alzheimer disease and normal controls by using neuropsychologic tests – Wechsler memory scale – revised (WMS-R), digit span subsets (digits forward and backward), trail making test B, Controlled oral word association test, animal Naming test, and 15 items version of the Boston naming test and it was concluded that many patients with COPD and mild hypoxemia who do not have neuropsychiatric histories may perform normally on cognitive measures. Oxygen therapy may partially account for presentation of cognitive function in these patients. Results also suggest that patients with COPD and normal controls can be readily distinguished from patients with mild Alzheimer disease based on levels and pattern of neuropsychologic test results. Any significant cognitive deficit in patients with mildly hypoxemic COPD may warrant continued neurologic evaluation.[5]

Reeves et al reported that impairment of pulmonary functions correlated significantly with the degree of alpha frequency slowing over the posterior cortical regions, and the slowest alpha frequencies occurred in those COPD patients with the lowest FEV1/FVC ratios. They concluded that the cognitive impairment was an important clinical consideration, but might go unrecognized until late in the course of the disease. This was a unique study using quantitative EEG (QEEG) analysis in these patients and had shown alpha asymmetry especially in severe COPD.[6] Hypoxemic patients with chronic obstructive pulmonary disease (COPD) have impaired cognitive performance and these neuropsychological impairments are related to the degree of hypoxemia. Cognitive performance in patients with non hypoxemic COPD was assessed and it was concluded that even non hypoxemic patients with COPD show significant impairments in cognitive performance.[7] Parekh and coresearchers examined the relationship between cognitive functioning and the severity of underlying lung disease in patients awaiting lung transplantation. And they concluded that Impaired neurocognitive functioning may be relatively common in patients awaiting lung transplantation and is associated with ineffective pulmonary gas exchange and reduced exercise tolerance.[8] Patients with Chronic Obstructive Pulmonary Disease (COPD) have relatively higher risk for cognitive impairment. There have been only a few research reports on cognitive impairment in COPD in India.

II. Methodology

The clinical study was conducted in Father Muller Medical College, Kankanady, Mangalore, which is a multi speciality hospital. All patients attending the out patient and inpatient facilities of the department of Medicine with a clinical diagnosis of chronic obstructive pulmonary disease constituted the population for the study. The study was conducted from the 1st September 2008 to the 31st of August 2010.The sample for the study consisted of thirty consecutive patients with chronic obstructive pulmonary disease who satisfied the inclusion and exclusion criteria.

Inclusion Criteria

- Patients with clinical diagnosis of COPD according to GOLD's criteria.
- Patients with at least Primary School Education.
- Male patients.
- Age group between 18 and 50 years

Exclusion Criteria

- Patients with COPD having other medical disorders like Diabetes Mellitus, Hypertension, thyroid and other endocrine disorders, renal failure other chronic debilitating medical conditions known to cause cognitive impairment.
- Patients with Psychiatric illness and substance dependence other than smoking.
- Patients who refused to give consent.

Consecutively selected 30 first degree male non affected relatives of COPD patients between age 18 and 50 years and 30 male patients with bronchial asthma between age 18 and 50 years who met the same inclusion and exclusion criteria constituted the control groups for the study.This study has been cleared by the institutional ethical committee. A written informed consent was obtained from all participants both in COPD patients and control groups. The socio demographic and clinical variables were recorded in a specific proforma prepared for this clinical study. All the participants underwent a thorough clinical examination to rule out medical disorders if any. Cognitive functions were assessed using Standardized Mini Mental Status Examination(SMMSE), Brief Cognitive Rating Scale(BCRS), Trail Making Test B (TMT-B), Digit Symbol Substitution Test(DSST).

III. Results

Table No. 1: Comparison of Age with cognitive function tests

		Age	N	Mean	Std. Deviation	P-value	
BCRS Total Score	COPD	18 – 40yrs	15	1.040	.0828	.000	HS
		41 – 50yrs	15	1.293	.1831		
		Total	30	1.167	.1899		
	Bronchial Asthma	18 – 40yrs	16	1.038	.1088	.163	NS
		41 – 50yrs	14	1.100	.1301		
		Total	30	1.067	.1213		
	Healthy Controls	18 – 40yrs	24	1.042	.1018	.226	NS
		41 – 50yrs	6	1.100	.1095		
		Total	30	1.053	.1042		
SMMSE Total Score	COPD	18 – 40yrs	15	29.067	1.387	.001	HS
		41 – 50yrs	15	26.600	2.292		
		Total	30	27.833	2.245		
	Bronchial Asthma	18 – 40yrs	16	29.562	1.031	.001	HS
		41 – 50yrs	14	27.786	1.672		
		Total	30	28.733	1.617		
	Healthy Controls	18 – 40yrs	24	29.458	.8836	.003	HS
		41 – 50yrs	6	28.000	1.4142		
		Total	30	29.1667	1.1472		
DSST Total Time	COPD	18 – 40yrs	15	398.667	40.1545	.000	HS
		41 – 50yrs	15	503.333	72.078		
		Total	30	451.000	78.228		
	Bronchial Asthma	18 – 40yrs	16	368.125	55.763	.197	NS
		41 – 50yrs	14	394.857	67.388		
		Total	30	382.000	62.223		
	Healthy Controls	18 – 40yrs	24	332.083	39.007	.009	HS
		41 – 50yrs	6	380.833	32.003		
		Total	30	341.833	42.159		
DSST error	COPD	18 – 40yrs	15	.6000	.9856	.001	HS
		41 – 50yrs	15	1.9333	1.4864		
		Total	30	1.2667	1.4126		
	Bronchial Asthma	18 – 40yrs	16	.3750	.8062	.001	HS
		41 – 50yrs	14	1.5714	.9376		
		Total	30	.9333	1.0482		
	Healthy Controls	18 – 40yrs	24	.3750	.5758	.001	HS
		41 – 50yrs	6	1.667	1.366		
		Total	30	.6333	.9279		
TMT – B Total time	COPD	18 – 40yrs	15	250.667	29.8727	.018	Sig
		41 – 50yrs	15	296.000	63.2229		
		Total	30	273.33	53.7768		
	Bronchial Asthma	18 – 40yrs	16	243.1250	50.427	.734	NS
		41 – 50yrs	14	237.8571	29.1359		
		Total	30	240.667	41.2673		
	Healthy Controls	18 – 40yrs	24	225.833	29.623	.063	NS
		41 – 50yrs	6	250.000	12.6491		
		Total	30	230.667	28.6396		
TMT-B Error	COPD	18 – 40yrs	15	.7333	1.0997	.042	Sig
		41 – 50yrs	15	1.667	1.2909		
		Total	30	1.200	1.2703		
	Bronchial Asthma	18 – 40yrs	16	.5000	.6325	.002	HS
		41 – 50yrs	14	1.5000	.9405		
		Total	30	.9667	.9279		
	Healthy Controls	18 – 40yrs	24	.16667	.3806	.012	Sig
		41 – 50yrs	6	.8333	.9832		
		Total	30	.30000	.5959		

Age wise comparison reveals that increasing age has a negative effect on cognitive functions, with the age group of 41 to 50 years performing worse than age group of 18 to 40 years on all the tests except TMT-B total time where in patients with bronchial asthma between age group 18 to 40 years performed worse than the age group 41 to 50 years. **(table 1)**

Marital status wise analysis reveals that single persons performed better on all the tests in all the groups except in bronchial asthma group where married persons performed well compare to singles in TMT-B total time. Group others which include divorced and widower performed worse in all the groups. There is highly significant difference in bronchial asthma group in the domains of BCRS total score ($p=0.001<0.01$), and SMMSE total score ($p=0.002<0.01$).There is significant difference in BCRS total score ($p=0.024<0.05$) and highly significant difference in SMMSE total score ($p=0.004<0.01$) in healthy control groups.

Table No. 2: Comparison of Educational Status with cognitive function tests

		Educational Status	N	Mean	Std. Deviation	P-value	
BCRS Total Score	COPD	Higher Professional/ MA/ Msc/BA/Bsc	11	1.727	1.348	.037	Sig
		Intermediate / Higher School/ Middle Pass/ Primary School	19	1.2210	1.988		
		Total	30	1.16667	.1899		
	Bronchial Asthma	Higher Professional/ MA/ Msc/BA/Bsc	11	1.03636	.08090	.306	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	19	1.0842	.138496		
		Total	30	1.06667	.121295		
	Healthy Controls	Higher Professional/ MA/ Msc/BA/Bsc	16	1.02500	.068313	.113	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	14	1.08571	.129241		
		Total	30	1.05333	.104166		
SMMSE Total Score	COPD	Higher Professional/ MA/ Msc/BA/Bsc	11	28.8181	2.2723	.066	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	19	27.2631	2.07744		
		Total	30	27.8333	2.24504		
	Bronchial Asthma	Higher Professional/ MA/ Msc/BA/Bsc	11	29.4545	1.21359	.062	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	19	28.3157	1.70139		
		Total	30	28.7333	1.6174		
	Healthy Controls	Higher Professional/ MA/ Msc/BA/Bsc	16	29.3750	.88506	.296	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	14	28.9285	1.384768		
		Total	30	29.1667	1.14721		
		Intermediate / Higher School/ Middle Pass/ Primary School	14	.71428	.72627		
		Total	30	.63333	.92785		
TMT Total Time	COPD	Higher Professional/ MA/ Msc/BA/Bsc	11	241.8182	34.0053	.012	Sig
		Intermediate / Higher School/ Middle Pass/ Primary School	19	291.5789	55.3035		
		Total	30	273.333	53.7768		
	Bronchial Asthma	Higher Professional/ MA/ Msc/BA/Bsc	11	248.1818	57.9341	.458	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	19	236.3158	28.7151		
		Total	30	240.6667	41.2672		
	Healthy	Higher Professional/ MA/ Msc/BA/Bsc	16	218.1250	20.4022	.008	HS
		Intermediate / Higher School/ Middle Pass/ Primary School	14	245.000	30.5714		
		Total	30	230.6667	28.6396		
TMT B error	COPD	Higher Professional/ MA/ Msc/BA/Bsc	11	.63636	1.02691	.063	NS
		Intermediate / Higher School/ Middle Pass/	19	1.526315	1.30675		

		Primary School					
		Total	30	1.2000	1.27035		
	Bronchial Asthma	Higher Professional/ MA/ Msc/BA/Bsc	11	.63636	.674199	.141	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	19	1.15789	1.01451		
		Total	30	.96667	.927857		
	Healthy	Higher Professional/ MA/ Msc/BA/Bsc	16	.125000	.34156	.085	NS
		Intermediate / Higher School/ Middle Pass/ Primary School	14	.5000	.759554		
		Total	30	.3000	.59596		

Education wise analysis reveals that highly educated persons performed better than persons with less education on all cognitive function tests. There is highly significant difference in DSST total time and significant difference in TMT-B total time and BCRS total score in cases. There is highly significant difference in DSST and TMT-B total time in healthy control group.(table 2).

Table No. 3: Comparison of Occupation with cognitive function tests

		Occupation	**N**	**Mean**	**Std. Deviation**	**P-value**	
BCRS Total Score	COPD	High Professional/ Semi professional	8	1.075000	.14880	.188	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	1.15555	21858		
		Semi Skilled Worker/ Unskilled Worker	13	1.23076	.179743		
		Total	30	1.16667	.189978		
	Bronchial Asthma	High Professional/ Semi professional	10	1.04000	.084327	.547	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	1.06000	.134989		
		Semi Skilled Worker/ Unskilled Worker	10	1.10000	.141421		
		Total	30	1.06667	.1212956		
	Healthy Controls	High Professional/ Semi professional	11	1.01818	.060302	.078	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	1.02500	.070710		
		Semi Skilled Worker/ Unskilled Worker	11	1.10900	.1375103		
		Total	30	1.05333	.1041660		
SMMSE Total Score	COPD	High Professional/ Semi professional	8	28.87500	2.41646	.126	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	28.2222	2.04803		
		Semi Skilled Worker/ Unskilled Worker	13	26.9230	2.05994		
		Total	30	27.8333	2.245045		
	Bronchial Asthma	High Professional/ Semi professional	10	29.4000	1.26491	.008	HS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	29.3000	1.33749		
		Semi Skilled Worker/ Unskilled Worker	10	27.5000	1.58113883		
		Total	30	28.7333	1.617433		
	Healthy Controls	High Professional/ Semi professional	11	29.45455	.820199	.286	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	29.37500	.916125		
		Semi Skilled Worker/ Unskilled Worker	11	28.72727	1.48935		
		Total	30	29.16667	1.147210		
DSST Total Time	COPD	High Professional/ Semi professional	8	400.000	68.86840	.063	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	452.2222	76.61229		
		Semi Skilled Worker/ Unskilled Worker	13	481.5385	73.2400		
		Total	30	451.000	78.22822		
	Bronchial Asthma	High Professional/ Semi professional	10	370.000	63.9442	.339	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	370.000	52.7046		
		Semi Skilled Worker/ Unskilled Worker	10	406.000	68.1827		

		Total	30	382.000	62.22318		
	Healthy Controls	High Professional/ Semi professional	11	320.9091	35.05839	.002	HS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	324.3750	35.09975		
		Semi Skilled Worker/ Unskilled Worker	11	375.4545	32.3615		
		Total	30	341.8333	42.15086		
DSST Error	COPD	High Professional/ Semi professional	8	.625000	1.40788595	.332	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	1.4444	1.81046		
		Semi Skilled Worker/ Unskilled Worker	13	1.5384615	1.050030		
		Total	30	1.26667	1.412587		
	Bronchial Asthma	High Professional/ Semi professional	10	.60000	.966091	.107	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	.70000	.94860		
		Semi Skilled Worker/ Unskilled Worker	10	1.50000	1.0801234		
		Total	30	.93333	1.64826		
	Healthy Controls	High Professional/ Semi professional	11	.272727	.46709	.259	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	.750000	1.48804		
		Semi Skilled Worker/ Unskilled Worker	11	.909090	.70064905		
		Total	30	.63333	.927857		
TMT Total Time	COPD	High Professional/ Semi professional	8	243.7500	35.0255	.035	Sig
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	260.000	46.36809		
		Semi Skilled Worker/ Unskilled Worker	13	300.7692	57.5125		
		Total	30	273.333	53.7768		
	Bronchial Asthma	High Professional/ Semi professional	10	250.000	60.5530	.662	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	233.000	25.4077		
		Semi Skilled Worker/ Unskilled Worker	10	239.000	31.7804		
		Total	30	240.667	41.2672		
	Healthy Controls	High Professional/ Semi professional	11	220.000	21.4476	.005	HS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	216.2500	18.46811		
		Semi Skilled Worker/ Unskilled Worker	11	251.8182	29.9393		
		Total	30	230.667	28.63965		
TMT B error	COPD	High Professional/ Semi professional	8	.62500	1.060660	.220	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	9	1.1111	1.69148		
		Semi Skilled Worker/ Unskilled Worker	13	1.61538	.96076		
		Total	30	1.2000	1.27035		
	Bronchial Asthma	High Professional/ Semi professional	10	.70000	.674948	.000	HS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	10	.40000	.5163977		
		Semi Skilled Worker/ Unskilled Worker	10	1.8000	.918936		
		Total	30	.96667	.927857		
	Healthy Controls	High Professional/ Semi professional	11	.0909091	.30151134	.057	NS
		Clerical shop/ Farm Owner/ Skilled worker/ Service Worker	8	.125000	.35355339		
		Semi Skilled Worker/ Unskilled Worker	11	.6363636	.8090398		
		Total	30	.30000	.595963		

Occupation based data shows that semiskilled/unskilled workers performed worse on all the cognitive function test in all the groups. There is highly significant difference in SMMSE total score and TMT-B error in bronchial asthma group. There is highly significant difference in healthy controls in DSST total time. There is significant difference in cases in TMT-B total time.(table 3).

Table No. 4: Comparison of substance use habbits with cognitive function tests

		Age	**N**	**Mean**	**Std. Deviation**	**P-value**	
BCRS Total Score	COPD	Smoking	16	1.1625000	.18211718	.759	NS
		Smoking and Alcohol	19	1.20000	.2236068		
		Nil	5	1.12000	.1788854		
		Total	30	1.16667	.1899788		
	Bronchial Asthma	Smoking	10	1.040000	.12649111	.055	NS
		Smoking and Alcohol	10	1.14000	.13498971		
		Nil	10	1.02000	.0632455		
		Total	30	1.06667	.1212959		

	Healthy Controls	Smoking	4	1.05000	.100000	.001	HS
		Smoking and Alcohol	5	1.20000	.14142136		
		Nil	21	1.019047	.06015852		
		Total	30	1.053333	.10416609		
SMMSE Total Score	COPD	Smoking	16	28.0625	1.948289	.845	NS
		Smoking and Alcohol	19	27.5556	2.788867		
		Nil	5	27.6000	2.5099800		
		Total	30	27.8333	2.24504		
	Bronchial Asthma	Smoking	10	28.8000	1.229272	.002	HS
		Smoking and Alcohol	10	27.5000	1.90029		
		Nil	10	29.9000	.31622777		
		Total	30	28.7333	1.617433		
	Healthy Controls	Smoking	4	28.5000	1.2909944	.006	HS
		Smoking and Alcohol	5	28.0000	1.5811388		
		Nil	21	29.57143	.746420003		
		Total	30	29.16667	1.147210		
DSST Total Time	COPD	Smoking	16	450.6250	75.5838386	.760	NS
		Smoking and Alcohol	19	463.3333	89.86100378		
		Nil	5	430.000	76.8114578		
		Total	30	451.000	78.22822		
	Bronchial Asthma	Smoking	10	383.000	52.291915	.012	Sig
		Smoking and Alcohol	10	421.000	61.18278		
		Nil	10	342.000	50.28805		
		Total	30	382.000	62.223180		
	Healthy Controls	Smoking	4	372.500	45.73474	.205	NS
		Smoking and Alcohol	5	352.000	41.47288		
		Nil	21	333.5714	40.408627		
		Total	30	341.8333	42.150864		
DSST error	COPD	Smoking	16	1.0625000	1.289379	.444	NS
		Smoking and Alcohol	19	1.77777	1.787300		
		Nil	5	1.00000	1.0000		
		Total	30	1.26667	1.412587		
	Bronchial Asthma	Smoking	10	.90000	.37559504	.003	HS
		Smoking and Alcohol	10	1.70000	1.0593499		
		Nil	10	.20000	.6324553		
		Total	30	.93333	1.0482607		
	Healthy Controls	Smoking	4	.50000	.5773502	.363	NS
		Smoking and Alcohol	5	1.0000	.7071067		
		Nil	21	.571428	1.028174		
		Total	30	.63333	.9278575		

TMT – B Total time	COPD	Smoking	16	262.000	48.37354	.422	NS
		Smoking and Alcohol	19	278.8189	58.61835		
		Nil	5	298.000	63.40346		
		Total	30	273.333	53.77689		
	Bronchial Asthma	Smoking	10	236.000	32.26665	.966	NS
		Smoking and Alcohol	10	243.000	31.64033		
		Nil	10	241.000	58.01340		
		Total	30	240.6667	41.26728		
	Healthy Controls	Smoking	4	250.000	50.33222	.201	NS
		Smoking and Alcohol	5	240.000	33.166247		
		Nil	21	224.7619	21.358615		
		Total	30	230.6667	28.63955		
TMT-B Error	COPD	Smoking	16	.937500	.997914	.485	NS
		Smoking and Alcohol	19	1.55555	1.1740051		
		Nil	5	1.40000	1.140175		
		Total	30	1.20000	1.2703515		
	Bronchial Asthma	Smoking	10	.900000	.875509	.001	HS
		Smoking and Alcohol	10	1.700000	.823272		
		Nil	10	.30000	.48304589		
		Total	30	.966667	.927857		
	Healthy Controls	Smoking	4	.00000	.00000	.089	NS
		Smoking and Alcohol	5	.80000	.8366600		
		Nil	21	.235095	.538958		
		Total	30	.30000	.5959634		

Substance use habbits data shows that persons who were using alcohol as well as smoking performed worse in all the three groups on all the cognitive function tests. There is highly significant difference in SMMSE total score, DSST error and TMT-B error and significant difference in DSST total time in bronchial asthma

group. There is highly significant difference in BCRS total score and SMMSE total score in healthy controls.(table 4).

Table No. 5: Comparison of Current Medications with cognitive function tests

		Current Medications	N	Mean	Std. Deviation	P-value	
BCRS Total Score	COPD	Bronchodilators	8	1.2000	1.0250	.011	Sig
		Steroids ,Bronchodilators and other medications	22	1.6000	1.2181		
		Total	30	1.6000	1.1667		
	Bronchial Asthma	Bronchodilators	21	1.0476	.1077	.194	NS
		Steroids ,Bronchodilators and other medications	9	1.1111	.1452		
		Total	30	1.0667	.1212		
SMMSE Total Score	COPD	Bronchodilators	8	29.1260	1.6420	.056	NS
		Steroids ,Bronchodilators and other medications	22	27.3636	2.2792		
		Total	30	27.833	2.2450		
	Bronchial Asthma	Bronchodilators	21	29.0952	1.261140	.060	NS
		Steroids ,Bronchodilators and other medications	9	27.888	2.08832		
		Total	30	28.733	1.6174		
DSST Total Time	COPD	Bronchodilators	8	397.500	47.1320	.021	Sig
		Steroids ,Bronchodilators and other medications	22	470.4545	48.8897		
		Total	30	451.000	48.2282		
	Bronchial Asthma	Bronchodilators	21	371.9048	67.7952	.179	NS
		Steroids ,Bronchodilators and other medications	9	405.556	40.6543		
		Total	30	382.00	62.2231		
DSST Error	COPD	Bronchodilators	8	.62500	1.1877	.136	NS
		Steroids ,Bronchodilators and other medications	22	1.500	1.4392		
		Total	30	1.2666	1.4125		
	Bronchial Asthma	Bronchodilators	21	.7619	.9952	.175	NS
		Steroids ,Bronchodilators and other medications	9	1.333	1.1180		
		Total	30	.9333	1.048		
TMT Total Time	COPD	Bronchodilators	8	243.7500	31.5942	.068	NS
		Steroids ,Bronchodilators and other medications	22	284.090	56.6239		
		Total	30	273.333	53.7768		
	Bronchial Asthma	Bronchodilators	21	239.0476	48.4669	.749	NS
		Steroids ,Bronchodilators and other medications	9	244.444	16.6667		
		Total	30	240.6667	41.2672		
TMT B error	COPD	Bronchodilators	8	.750000	1.1649	.249	NS
		Steroids ,Bronchodilators and other medications	22	1.3636	1.2926		
		Total	30	1.2000	1.2703		
	Bronchial Asthma	Bronchodilators	21	.8095	.8728	.160	NS
		Steroids ,Bronchodilators and other medications	9	1.333	1.000		
		Total	30	.9667	.9278		

Patients who are only on bronchodilators have less cognitive impairment compared to patients who are on steroids and bronchodilators.This difference is statistically significant in COPD patients.(table 5).

Table No. 6: Comparison of Staging of COPD or Spirometry with cognitive function tests

		Age	N	Mean	Std. Deviation	P-value	
BCRS Total Score	COPD	Stage I	15	1.06667	0.1234	0.000	HS
		Stage II	10	1.18000	0.1751		
		Stage III and IV	5	1.44000	0.0894		
		Total	30	1.16667	0.1899		
SMMSE Total Score	COPD	Stage I	15	28.9333	1.38701	0.004	HS
		Stage II	10	27.4000	2.4129		
		Stage III and IV	5	25.4000	2.0736		
		Total	30	27.8593	2.2450		
DSST Total Time	COPD	Stage I	15	400.52	48.2355	0.000	HS

		Stage II	10	462.000	68.6051		
		Stage III and IV	5	566.000	31.3049		
		Total	30	451.000	78.2282		
DSST error	COPD	Stage I	15	0.66000	0.9856	0.025	Sig
		Stage II	10	1.8000	1.3984		
		Stage III and IV	5	2.2000	1.7885		
		Total	30	1.2667	1.4125		
TMT – B Total time	COPD	Stage I	15	247.333	30.5816	0.001	HS
		Stage II	10	278.000	49.8442		
		Stage III and IV	5	342.000	60.1666		
		Total	30	273.333	53.7768		
TMT-B Error	COPD	Stage I	15	0.7333	1.0997	0.032	Sig
		Stage II	10	1.3000	1.0593		
		Stage III and IV	5	2.4000	1.5165		
		Total	30	1.2000	1.2703		

COPD patients in the stage III and IV performed worse on all the cognitive tests. There is highly significant difference in BCRS total score, SMMSE total score, DSST total time and TMT-B total time .There is significant difference in DSST error and TMT-B error.(table 6).

Table No. 7: Relation between duration of illness and cognitive function tests

		Duration of illness	**N**	**Mean**	**Std. Deviation**	**P-value**	
BCRS Total Score	COPD	2 to 5 yrs	13	1.03076	.07510	.000	HS
		5- 10 yrs	8	1.22500	.19820		
		More than 10yrs	9	1.311111	.17638		
		Total	30	1.6667	.18997		
	Bronchial Asthma	2 to 5 yrs	12	1.01667	.057735	.048	HS
		5- 10 yrs	10	1.06000	.13498		
		More than 10yrs	8	1.15000	.14142		
		Total	30	1.06667	.121295		
SMMSE Total Score	COPD	2 to 5 yrs	13	29.000	1.471901	.001	HS
		5- 10 yrs	8	28.25000	1.66904		
		More than 10yrs	9	25.7778	2.3333		
		Total	30	27.8333	2.24504		
	Bronchial Asthma	2 to 5 yrs	12	29.75000	.62158	.004	HS
		5- 10 yrs	10	28.5000	1.50923		
		More than 10yrs	8	27.5000	1.92724		
		Total	30	28.7333	1.6174		
DSST Total Time	COPD	2 to 5 yrs	13	402.3077	41.2621	.001	HS
		5- 10 yrs	8	451.2500	90.4650		
		More than 10yrs	9	521.111	55.5527		
		Total	30	451.000	78.2282		
	Bronchial Asthma	2 to 5 yrs	12	353.333	54.3278	.004	HS
		5- 10 yrs	10	391.000	74.1544		
		More than 10yrs	8	413.750	40.6860		
		Total	30	382.000	62.2231		
DSST error	COPD	2 to 5 yrs	13	.61538	1.04390	.001	HS
		5- 10 yrs	8	1.62500	1.68501		
		More than 10yrs	9	1.8889	1.36422		
		Total	30	1.26667	1.41258		
	Bronchial Asthma	2 to 5 yrs	12	.58333	1.0836	.085	HS
		5- 10 yrs	10	.7000	.82327		
		More than 10yrs	8	1.75000	.88640		
		Total	30	.93333	1.04826		
TMT – B Total Time	COPD	2 to 5 yrs	13	250.000	31.0912	.078	HS
		5- 10 yrs	8	278.750	51.9443		
		More than 10yrs	9	302.222	69.4222		
		Total	30	273.333	53.7768		
	Bronchial Asthma	2 to 5 yrs	12	240.8333	55.6708	.998	HS
		5- 10 yrs	10	240.000	35.5902		
		More than 10yrs	8	241.2500	23.5660		
		Total	30	240.667	41.2672		
TMT – B error	COPD	2 to 5 yrs	13	.76923	1.16775	.123	HS
		5- 10 yrs	8	1.12500	1.7268		
		More than 10yrs	9	1.8889	.60092		
		Total	30	1.2000	1.27035		
	Bronchial Asthma	2 to 5 yrs	12	.66667	.887625	.055	HS
		5- 10 yrs	10	.80000	.91893		
		More than 10yrs	8	1.625000	.7440		

		Total	30	.96667	.92785		

Duration of illness wise analysis reveals that there is highly significant difference in the BCRS total score, (P = 0.00 <.01), SMMSE total score, DSST total time, DSST error in cases. In bronchial asthma there is highly significant difference in SMMSE total score and DSST total time. There is no significant difference found in the domains of TMT – B Total time and TMT –B error in all the three groups.This indicates if duration of illness is more than there is more cognitive impairment in both the cases and bronchial asthma group (table 7).

IV. Discussion

The three samples do not significantly differ in terms of age, marital status, religion, domicile distribution, occupation and income. This fact indicates that the chronic obstructive pulmonary disease (COPD) patients and the two control groups are matched. In the case of education there is significant difference among the patients and both the control groups. The healthy individuals have significantly better educational status when compared to that of patients with bronchial asthma and COPD . Such findings are not reported in literature reviewed. It could be possible that the poorer education status in both groups of patients may be attributable to the chronic states of the respiratory diseases and their consequences.

About fifty percent of COPD patients and 33% bronchial asthma patients are smoking and using alcohol whereas 70% of healthy controls do not use them. The difference is statistically significant. It is likely that smoking is one of the causes for COPD and bronchial asthma, rather than the consequences. Smoking is one of the major risk factor in COPD patients.[9] There is no statistically significant difference with respect to duration of illness in COPD patients and patients with bronchial asthma. A significant proportion of patients of COPD are on steroids as well as bronchodilaters, whereas only thirty percent patients of bronchial asthma are on steroids. An earlier study on psychopathology in COPD patients postulates that the medication could be related to psychopathology.[10] But the nature of medications and the dosage of medications are not mentioned. Spirometry done on COPD patients reveals that fifty percent belongs to stage I and about thirty three percent belongs to stage II. Thirty percent patients with bronchial asthma had family history of psychiatric medial or substance use disorders, whereas no significant family history is reported in COPD patients. Present investigation finds that cognitive impairment assessed with most of the neuropsychological tests are present in a significant proportion of patients with COPD.It is found that attention, speed of performance ,visual scanning,sequential abilities,executive function,psychomotor performance ,perceptual organization are impaired in these patients. Presence of cognitive impairment has been documented in verbal processing, attention, deductive thinking, drawing skills, passive recognition, active recall abstract, reasoning, memory, language, speed of performance., mental flexibility, delayed recall and impairment in verbal memory.[3,5,11] It is postulated that these problems may be attributed to the direct effects of hypoxia, hypercapnia, hyperventilation, respiratory failure, COPD exacerbation ,smoking, and medications.[10] Both COPD and smoking generates hypoxia leading to neuropsychiatric disturbances in these patients. The other factor which may contribute to cognitive dysfunction in COPD is comorbid psychopathology. The result of the present study indicates that there is significant cognitive impairment in patients with COPD. Results of the present study are consistant with the reports of earlier investigations.[1,2,3,5,10,11,12,13,14,15,16,17]

In the current study the total mean score obtained by COPD on SMMSE is 27.83, bronchial asthma group scored 28.73 and healthy controls scored 28.73. There is statistically significant difference between these three group on total SMMSE score and recall domaine of SMMSE. Highly significant difference is found in the doman of attention , where COPD patients scoring the lowest score, followed by bronchial asthma controls. Multiple comparison analysis reveals that there is highly significant difference in the domain of attention between COPD patients and bronchial asthma patients and between COPD patients and healthy controls, However there is no statistically significant difference found between bronchial asthma and healthy controls. It is found that significant difference exists between COPD and bronchial asthma patients , and between COPD and healthy controls in the domain of recall, however there is no statistically significant difference between bronchial asthma and healthy controls. In total SMMSE there is no significant difference between COPD patients and bronchial asthma and between bronchial asthma and healthy controls. But there is significant

difference between COPD patients and healthy controls . A cut of score of less than 24 on SMMSE is indicative of cognitive impairment. In this study there is no cognitive impairment found based on SMMSE,

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 relavant input ability to solve abstract problems, psychomotor speed and visuo spatial ability.

To overcome this limitation this study has employed BCRS, TMT-B and DSST to assess cognitive functions in detail.

The brief cognitive rating scale is used primarily as a measure of cognitive decline and may not be appropriate for a cross sectional comparative study such as this study. Earlier studies have not used BCRS to evaluate cognitive impairment in COPD. In this study statistically highly significant difference is found in the domain of recent memory and total BCRS score . The COPD group have higher mean score indicating cognitive impairment in these patients. Multiple comparison analysis reveals that there is statistically highly significant difference between COPD and bronchial asthma group and between COPD and healthy controls , but there is no significant difference between bronchial asthma group and healthy controls in the domain of recent memory. There is significant difference in COPD and bronchial asthma group and healthy controls in the domain of recent memory. There is significant difference in COPD and bronchial asthma group in total BCRS score , but there is no difference between bronchial asthma and healthy controls in total BCRS scores. This indicates that COPD group has cognitive impairment based on BCRS, which is more than the bronchial asthma group. However there is no significant difference between bronchial asthma and healthy controls but bronchial asthma group have higher mean score values compared to healthy controls, indicating more cognitive impairment but less than the COPD group.

The current study employed two domain specific tests, TMT–B,and DSST to comprehensively assess cognitive function which is one of the merits of this study. In present study TMT – B reveals presence of cognitive impairment in COPD patients followed by bronchial asthma group. TMT – B is more sensitive to cognitive dysfunction than SMMSE and hence its use helps to detect subtle cognitive decline. In this study there is highly significant difference between three groups in time taken to complete the DSST but there is no significant difference found in the number of errors made. DSST reveals that there is cognitive important in COPD patients followed by bronchial asthma group.

Present study finds that older patients tend to have more cognitive deficits.It is found that the less educated patients have more cognitive impairment.similar findings are reported in earlier studies.[2,,11,18] This study shows that subject employed as semiskilled / unskilled labours have more cognitive impairment compared to high / semi professional or clerical or skilled workers. Present study shows that single persons performed better on almost all the cognitive tests. Widowers / separated and divorced performed worse in all the groups. But this difference is not statistically significant in COPD patients.

Present investigation shows that persons who are using alcohol as well as smoking have worst performance in the three groups on all the cognitive functions. This finding is consistent with that of earlier studies .[1,19,20] Present study shows that duration of illness is significantly related to cognitive impairment in patients with COPD and bronchial asthma. Present study reveals that COPD patients with GOLD stage III and IV performed worse on all the cognitive function tests.

Airway obstruction resulting in hypoxia is a key feature in COPD patients, and it is the basis of Gold's COPD staging as evidenced by FEV_1.Hypoxia has detrimental effects on cognitive functions ,both smoking and COPD generates hypoxia leading to cognitive impairment. The findings of the current study are consistent with those of earlier studies.[2,3,4,7,8,14,15,16,21,22] Severity of COPD is also related to cognitive impairment in the same way. Other studies also report the same.[15,18] Present investigation reveals that cognitive impairment is significantly related to steroids in COPD patients

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