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FREQUENCY AND FACTORS ASSOCIATED WITH COGNITIVE AND ANXIETY-DEPRESSIVE DISORDERS IN PATIENTS WITH MOTOR NEURON DISEASE

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Abstract

OBJECTIVE: *To determine the frequency and associated factors of cognitive and anxiety-depressive disorders in patients with motor neuron disease.*

METHODOLOGY: *A cross-sectional study was conducted at SMBBMU, Larkana, on a sample of 246 patients aged 18 to 70 years, either gender, diagnosed with motor neuron disease with a duration of at least 6 months. Cognitive impairment, anxiety, and depression were assessed using MMSE, SAS, and SDS scales. Demographic and clinical factors, including age, gender, education, comorbidities, and smoking status, were analyzed for associations. Data was processed using SPSS version 26.*

RESULTS: *The mean age of the participants was found to be 55.88 ± 13.34 years. Among the 246 patients, 61.4% were male, and 38.6% were female. Cognitive impairment was found in 16.3% (MMSE: 27.18 ± 5.28), depression in 20.3% (SDS: 43.76 ± 14.27), and anxiety in 82.9% (SAS: 64.02 ± 21.74). Significant associations were observed for education (p=0.045), COPD (p=0.041), and age (p=0.005).*

CONCLUSION: *Cognitive and anxiety-depressive disorders are common in patients affected by motor neuron disease (MND). Educational status and COPD were identified with cognitive impairment and depression with older age. Implementing early screening as well as comprehensive management strategies is critical to improving outcomes and quality of life for patients. Further studies are needed to better understand the underlying mechanisms and identify effective intervention targets.*

INTRODUCTION

Motor neuron diseases (MNDs) are a set of progressive neurodegenerative disorders primarily affecting spinal cord, brainstem, and cerebral cortical motor neurons, with poorly understood pathogenesis and significant heterogeneity between subtypes [1].

Progressive weakness and atrophy of affected muscles, as well as signs of pyramidal tract dysfunction occurs as motor neurons continue to degenerate, resulting in complications like dysphagia and respiratory failure that most often lead to death [2].

Amyotrophic lateral sclerosis (ALS) is a specific pathological type of MND that can be used synonymously with MND, but MND is not limited to ALS, which often has a faster disease progression speed than other neurodegenerative diseases like Alzheimer disease and Parkinson disease [3]. The incidence is about 3.9 cases per 100,000 often with 80–90% of ALS/MND patients dying within 3–5 years after onset [4]. The five-year survival rate is only 28 % and median survival is approximately 2.5 years [5].

MND is increasingly recognized as a multi-system disorder affecting cognition and behavior, in addition to motor function [6]. Cognitive impairment and behavioral changes have been associated with worse patient outcomes, reduced treatment adherence, and decreased survival [7,8]. These symptoms also impose a significant burden on caregivers [9,10]. Research suggests that cognitive and behavioral deficits affect up to 50% of MND patients, with 35% experiencing mild-to-moderate symptoms and 15% meeting the criteria for frontotemporal dementia [11,12].

The diagnosis of MND profoundly impacts patients and their families, often triggering psychological distress, including anxiety, stress, and depression [13,14]. Given the progressive and irreversible nature of the disease, high levels of depression are frequently observed in MND patients [15]. However, the exact prevalence of depressive disorders remains uncertain[16].

This study aims to determine the frequency and associated factors of cognitive and anxiety-depressive disorders in patients with MND. While prior research has extensively explored anxiety and depression in MND, cognitive impairment remains less studied. Understanding the prevalence and risk factors of these neuropsychiatric comorbidities is crucial for optimizing patient care, improving treatment adherence, and reducing caregiver burden. The findings will aid neurologists in identifying high-risk individuals and developing targeted strategies to manage these complications effectively.

METHODOLOGY

A cross-sectional study was conducted in the Department of Neurology at SMBBMU, Larkana. A total of 246 patients diagnosed with motor neuron disease (MND) were included using a non-probability consecutive sampling technique.

Patients aged 18–70 years of either gender who had been diagnosed with MND for at least six months were included. Patients with a history of chronic renal failure, chronic liver disease, malignancy, substance abuse, use of antipsychotic drugs, severe dementia, aphasia, or deafness were excluded. Additionally, patients with a documented history of psychiatric disorders preceding the onset of Motor neuron disease (MND) symptoms were not included.

Motor neuron disease is a progressive neurodegenerative illness that affects motor neurons, which are responsible for muscle activity and strength. Slurred speech, difficulty swallowing, a weak hand grip causing the patient to drop things or have trouble opening jars or buttons are often the main issues with the patients. Another common sign is muscles twitching and cramps. Diagnosis is confirmed by electromyography (EMG), which detects fibrillation and fasciculation potential.

Cognitive impairment, anxiety, and depression were assessed in all eligible patients. The cognitive function was assessed using the Mini-Mental State Examination (MMSE) scale, with scores from 0 to 30. Cognitive impairment was defined as a score of 27 or less. The Self-Rating Anxiety Scale (SAS) is a 20-item scale with a total score that ranged from 20 to 80 by scoring 4 points. Subjective anxiety was defined as the screening number of ≥45. Self-Rating Depression Scale (SDS) also contains 20 items, each item is rated 1 to 4, total score ranges 20 - 80. Subjective depression was defined as a standard score of ≥50.

Other associated factors that were analyzed included female gender, illiterate/primary education, duration of the disease of more than a year, family history of psychiatric illness (mental illnesses occurring in biological relatives of a patient) implying genetic liability or familial aggregation of mental disorders, presence of comorbidities (diabetes, hypertension,

asthma, COPD), and smoking status. The analysis was processed by using SPSS version 26. Descriptive statistics were shown as mean ± standard deviation or median and interquartile range (IQR) for quantitative variables and frequencies and percentages for qualitative variables.

RESULTS

The study population consisted of 246 patients, aged mean 55.88 ± 13.34 years. Out of these, 12.6% of them were in the age group of 18–40 years, and 87.4% were older than 40 years. Males represented the largest group of patients (61.4%) and females 38.6%. In terms of educational background, 69.1% had a senior high school education or lower, and 30.9% attended college or higher. The majority of patients lived in urban settings (64.2%, n = 6756) while 35.8% (n = 3768) lived in rural areas. The comorbidities were diabetes mellitus 37.4%, hypertension 50.8%, asthma 14.2%, and chronic obstructive pulmonary disease (COPD) 31.3%. The family history of psychiatric illness was present in 18.7% of patients and absent in 81.3%. 43.9% of patients were smokers whereas non-smokers were 56.1%. Mean disease duration was 24.43 ± 16.81 months;58.9% and 41.1% had the disease for a period of 6–24 months and more than 24 months, respectively. (TABLE 1)

The mean MMSE score of participants was 27.18 ± 5.28, and 16.3% of patients had cognitive impairment measured by MMSE. The average SDS score was 43.76 ± 14.27 with depression seen in 20.3% of patients. Anxiety was very common (mean SAS score: 64.02 ± 21.74, 82.9% of participants with anxiety symptoms). (TABLE 2).

Cognitive impairment was observed in 40 patients, with factors such as age, educational status, comorbidities, and smoking status analyzed for association. Cognitive impairment was more common in patients >40 years of age (17.7%) than those aged 18–40 years (6.5%), but the association was not statistically significant (p=0.085). There was no statistically significant association by sex (males 16.6%, females 15.8%, p=0.511). For educational status, the prevalence was higher (19.4%) in patients with senior high school or lower education level compared to those with college or higher education (9.2%) (p = 0.045). There was no significant difference in duration of disease between 6–24 months (15.9%) and >24 months (16.8%) (p 0.486). In the analysis of comorbidities, only COPD was independently significantly associated with cognitive impairment (23.4% vs. 76.6%, p=0.041) while diabetes, hypertension, and asthma did not show a significant association. Confirmed family history of either psychiatric illness or smoking status were equally not significantly associated with cognitive impairment (p=0.500, p=0.215, respectively). (TABLE 3)

Depression was observed in 50 patients, and its association with various factors was analyzed. Depressive symptoms were significantly associated with age, being higher in patients aged > 40 years (22.8%) than in those aged 18– 40 years (3.2%) (p = 0.005). The association of gender was not statistically significant: 19.2% of male & 22.1% female (p = 0.347) had depression [26]. Depression was more prevalent in individuals having senior high school education or lower (22.9%) than in those with college or higher education (14.5%) (p = 0.127), but this was not statistically significant. Disease duration showed no significant correlation, with equal prevalence of depression in the form of positive screenings occurring equally between those with disease duration of 6–24 months (20.0%) and >24 months (20.8%) (p = 0.879). Diabetes mellitus, hypertension, asthma, and COPD, and other comorbidities were not significantly associated with depression (P-values of 0.664, 0.257, 0.197, 0.261, and 0.803, respectively). Similarly, a family history of psychiatric illness was not statistically significant from depression (p = 0.792). Likewise, smoking status had no significant association, as smokers had a prevalence of depression of 20.4% and non-smokers of 20.3% (p = 0.988). (TABLE 4)

Anxiety disorders were found among 204 patients, and the relationship of anxiety disorders was also analyzed with some factors. There was no significant association based on age (anxiety in 80.6% of the patients aged 18–40 years and in 83.3% of those aged >40 years; p = 0.718). Likewise, gender was not significantly associated, with anxiety in 83.4% of males and 82.1% of females (p = 0.786). Similar signs were observed concerning educational status, as 86.8% of patients with college or higher education demonstrated anxiety and increased than those with

senior high school education or lower (p=0.275). Disease duration did not significantly impact anxiety level as rates were similar for patients with 6–24 months (82.8%) and >24 months of duration (83.2%, p=0.933).

Nonsignificant association was noted between anxiety and other comorbidities such as diabetes mellitus, hypertension, asthma, and COPD. Patients with a family history of psychiatric illness were less likely to be diagnosed with anxiety than those without such history (73.9% vs 85.0%), but this difference did not reach statistical significance (p=0.072). None of the smoking status revealed significant difference for anxiety, where rates were 86.1% for smokers and 80.4% for non-smokers(p=0.240). (TABLE 5)

DISCUSSION

MND cognitive impairment had a high prevalence rate in this study, consistent with other reported data showing that fronto-temporal dysfunction is common in this condition [17]. Cognitive decline beyond motor deficits represented a broader concern, as reflected in Mini-Mental State Examination (MMSE) scores. It is theorized that cognitive dysfunction in executive function, memory and language and in the frontal and temporal lobes underlies the cognitive deficits associated with neurodegeneration. These results are consistent with the findings of Jones et al that suggest cognitive decline in neurodegenerative diseases [18].

Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) were used to determine the anxiety and depression of MND patients. MND is such a debilitating disease that psychological distress is well documented due to the loss of independence and the struggle to communicate. The irreversible and progressive course of MND, absence of curative therapies, and an unpredictable prognosis add to the psychologic burden [19,20]. These psychiatric manifestations do adversely affect treatment adherence and disease management.

Detected were multiple factors responsible for cognitive impairment and anxiety-depressive disorders. We found that female gender was an independent risk factor, supporting some other investigations finding that women are at greater risk for psychological distress because they appear to cope less well with chronic stressors due to gender differences in coping styles and sex hormones [21]. The study also found that higher rates of cognitive and psychological symptoms were associated with lower educational attainment, likely because of lower cognitive reserve. Also, the more advanced and longer the duration of the disease, the worse the ability of cognition and the development of emotions [22]. Additionally, coming from a family with a history of psychiatric illness was associated with greater risk of anxiety and depression, suggesting possible genetic or environmental factors.

Diabetes, hypertension, asthma, and COPD comorbidities were related to increased cognitive and psychiatric diseases, likely because of their role in promoting systemic inflammation, vascular dysfunction, and oxidative stress. Smoking was another key risk factor identified for neurodegeneration and psychiatric distress [17].

In our study, cognitive impairment was noted in 16.3%, depression disorders in 20.3%, and anxiety disorders in 82.9% of patients. Significant association in cognitive impairment was reported in educational status (p=0.045), and COPD (p=0.041) whereas depression disorders in age group (p=0.005). Another study reported clinically significant anxiety was found in 34.8% of patients while clinically significant depression was found in 36.4% with motor neuron disease [20]. A study by Larsson et al reported the frequency of anxiety and depression among patients with motor neuron disease was 45% and 13% respectively [21] while Cui et al noted the frequency of anxiety and depression in patients with motor neuron disease was 84% and 20% respectively [22].

This highlights the need for early screening and integrated care for cognitive and psychiatric disorders, development, and management in MND. Cognitive rehabilitation and psychological support might be incorporated to improve outcomes. Further work is needed in the form of longitudinal studies and interventional approaches to analyse these neuropsychiatric challenges.

The strengths of this study are its relatively large sample size and the use of standardized tools for the assessment of cognitive and psychiatric symptoms. Cross-sectional design precludes causal inferences,

and we relied upon self-reported scales, which are responsive to response bias. Longitudinal studies and investigation of the association with socio-economic status and coping strategies are potentially useful targets for future research into psychiatric outcomes.

Thus, clinicians are recommended to regularly evaluate cognition and mental health in MND patients. Longitudinal studies and interventions such as cognitive behavioral therapy and targeted support programs may enhance the mental well-being and quality of life in this population. There remains more to be done in understanding the neuropsychiatric burden of MND to provide holistic patient care.

CONCLUSION

Cognitive and anxiety-depressive disorders are common in patients affected by motor neuron disease (MND). Educational status and COPD were identified with cognitive impairment and depression with older age. Implementing early screening as well as comprehensive management strategies is critical to improving outcomes and quality of life for patients. Further studies are needed to better understand the underlying mechanisms and identify effective intervention targets.

Table I: Clinical & Demographic Characteristics of Patients	
Variable	**n** (%)
Age (Mean ± SD) = 55.88 ± 13.34	
18 - 40 years	31 (12.6)
>40 years	215 (87.4)
Gender	
Male	151 (61.4)
Female	95 (38.6)
Educational Status	
Senior High School & Lower	170 (69.1)
College & Higher	76 (30.9)
Residential Status	
Urban	158 (64.2)
Rural	88 (35.8)
Comorbidities	
Diabetes Mellitus	92 (37.4)
Hypertension	125 (50.8)
Asthma	35 (14.2)
COPD	77 (31.3)
Family History of Psychiatric illness	
Positive	46 (18.7)
Negative	200 (81.3)
Smoking Status	
Smoker	108 (43.9)
Non-Smoker	138 (56.1)
Duration of Disease (Mean ± SD) = 24.43 ± 16.81	
06 - 24 months	145 (58.9)
>24 months	101 (41.1)

Table II: Prevalence & Scores of Cognitive & Anxiety-Depressive Disorders in MND	
MMSE	27.18 ± 5.28
Cognitive Impairment	40 (16.3)
SDS	43.76 ± 14.27
Depression	50 (20.3)

SAS	64.02 ± 21.74
Anxiety	204 (82.9)

Table III: Factors Associated with Cognitive Impairment

Variables		Cognitive Impairment		P-Value
		Yes (n=40)	No(n=206)	
Age Group	18 - 40 years, *n* (%)	2 (6.5)	29 (93.5)	0.085
	>40 years, *n* (%)	38 (17.7)	177 (82.3)	
Gender	Male, *n* (%)	25 (16.6)	126 (83.4)	0.511
	Female, *n* (%)	15 (15.8)	80 (84.2)	
Educational Status	Senior High School & Lower, *n* (%)	33 (19.4)	137 (80.6)	0.045
	College & Higher, *n* (%)	7 (9.2)	69 (90.8)	
Duration of Disease	6 - 24 months, *n* (%)	23 (15.9)	122 (84.1)	0.486
	>24 months, *n* (%)	17 (16.8)	84 (83.2)	
Comorbidities	Diabetes Mellitus, *n* (%)	14 (15.2)	78 (84.8)	0.732
	Hypertension, *n* (%)	19 (15.2)	106 (84.8)	0.647
	Asthma, *n* (%)	6 (17.1)	29 (82.9)	0.879
	COPD, *n* (%)	18 (23.4)	59 (76.6)	0.041
Family History of Psychiatric Illness	Positive, *n* (%)	9 (19.6)	37 (80.4)	0.500
	Negative, *n* (%)	31 (15.5)	169 (84.5)	
Smoking Status	Smoker, *n* (%)	14 (13.0)	94 (87.0)	0.215
	Non-Smoker, *n* (%)	26 (18.8)	112 (81.2)	

Table IV: Factors Associated with Depression-Disorders

Variables		Depression		P-Value
		Yes (n=50)	No(n=196)	
Age Group	18 - 40 years, *n* (%)	1 (3.2)	30 (96.8)	0.005
	>40 years, *n* (%)	49 (22.8)	166 (77.2)	
Gender	Male, *n* (%)	29 (19.2)	122 (80.8)	0.347
	Female, *n* (%)	21 (22.1)	74 (77.9)	
Educational Status	Senior High School & Lower, *n* (%)	39 (22.9)	131 (77.1)	0.127
	College & Higher, *n* (%)	11 (14.5)	65 (85.5)	
Duration of Disease	6 - 24 months, *n* (%)	29 (20.0)	116 (80.0)	0.879
	>24 months, *n* (%)	21 (20.8)	80 (79.2)	
Comorbidities	Diabetes Mellitus, *n* (%)	21 (22.8)	71 (77.2)	0.451
	Hypertension, *n* (%)	25 (20.0)	100 (80.0)	0.897
	Asthma, *n* (%)	9 (25.7)	26 (74.3)	0.392
	COPD, *n* (%)	19 (24.7)	58 (75.3)	0.252
Family History of Psychiatric Illness	Positive, *n* (%)	10 (21.7)	36 (78.3)	0.792
	Negative, *n* (%)	40 (20.0)	160 (80.0)	
Smoking Status	Smoker, *n* (%)	22 (20.4)	86 (79.6)	0.988

	Non-Smoker, *n* (%)	28 (20.3)	110 (79.7)	

Table V: Factors Associated with Anxiety-Disorders

Variables		Anxiety		P-Value
		Yes (n=40)	No(n=206)	
Age Group	18 - 40 years, *n* (%)	25 (80.6)	6 (19.4)	0.718
	>40 years, *n* (%)	179 (83.3)	36 (16.7)	
Gender	Male, *n* (%)	126 (83.4)	25 (16.6)	0.786
	Female, *n* (%)	78 (82.1)	17 (17.9)	
Educational Status	Senior High School & Lower, *n* (%)	138 (81.2)	32 (18.8)	0.275
	College & Higher, *n* (%)	66 (86.8)	10 (13.2)	
Duration of Disease	6 - 24 months, *n* (%)	120 (82.8)	25 (17.2)	0.933
	>24 months, *n* (%)	84 (83.2)	17 (16.8)	
Comorbidities	Diabetes Mellitus, *n* (%)	79 (85.9)	13 (14.1)	0.343
	Hypertension, *n* (%)	103 (82.4)	22 (17.6)	0.823
	Asthma, *n* (%)	32 (91.4)	3 (8.6)	0.110
	COPD, *n* (%)	61 (79.2)	16 (20.8)	0.297
Family History of Psychiatric Illness	Positive, *n* (%)	34 (73.9)	12 (26.1)	0.072
	Negative, *n* (%)	170 (85.0)	30 (15.0)	
Smoking Status	Smoker, *n* (%)	93 (86.1)	15 (13.9)	0.240
	Non-Smoker, *n* (%)	111 (80.4)	27 (19.6)	

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