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SPECTRUM OF DEMYELINATING DISEASES IN PAKISTAN: A MULTICENTER CROSS-SECTIONAL STUDY

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ABSTRACT

Background and Objective:

Demyelinating diseases are a heterogeneous group of disorders of the central nervous system, including multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and acute disseminated encephalomyelitis (ADEM). Data from South Asia remain scarce, despite potential regional variations in disease spectrum and outcomes. The objective of this study was to characterize the demographic, clinical, and disability profile of patients with demyelinating disorders across Pakistan.

Methods:

This multicenter cross-sectional study was conducted between August 2017 and December 2019 across 39 neurology centers in Pakistan. Adult patients (≥18 years) diagnosed with demyelinating disorders using standardized criteria were included. Data on demographics, education, comorbidities, and disability (modified Rankin Scale) were collected. Statistical analyses were performed using t-tests and chi-square tests, with significance set at $p<0.05$.

Results:

A total of 373 patients were analyzed (59.5% female; mean age 37.2 ± 11.7 years). MS was the most frequent diagnosis (79.1%), followed by NMOSD (11.8%), ADEM (5.1%), and leukodystrophy (4.0%). Females had higher MS prevalence (82.9% vs. 73.5%, p=0.02) and higher rates of illiteracy. Hypertension (9.4%) and diabetes (6.7%) were more common in older and male patients. While 33.5% were fully functional, 16.7% had moderate-to-severe disability, including 6.7% who were bedridden.

Conclusion:

Demyelinating diseases in Pakistan predominantly affect young adults, with MS as the leading disorder but NMOSD comprising a notable proportion. Female predominance, education disparities, and significant disability highlight the need for improved diagnostic access, equitable treatment, and targeted rehabilitation strategies in South Asia.

Keywords: Demyelinating diseases; Multiple sclerosis; Neuromyelitis optica; Acute disseminated encephalomyelitis; Disability;

INTRODUCTION

Demyelinating diseases are disorders affecting either the

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central or peripheral nervous system characterized by destruction of the myelin sheath and relative preservation of the axon.[1] The integrity of myelin is critical for saltatory conduction and efficient transmission of nerve impulses; hence, its loss can result in a wide spectrum of neurological dysfunction depending on the site and extent of involvement. These disorders should be distinguished from those in which there is a failure of myelination, referred to as dysmyelination.[2] Dysmyelinating conditions are usually genetic or developmental in nature, whereas demyelination typically represents an acquired pathological process.

The spectrum of acquired demyelinating diseases of the central nervous system is diverse, based on the pathogenesis, and ranges from autoimmune inflammatory etiologies such as multiple sclerosis and neuromyelitis

optica spectrum disorder to post-infectious causes such as acute disseminated encephalomyelitis. In addition, demyelination may also occur because of metabolic disturbances, exemplified by osmotic demyelination syndrome, or following hypoxic-ischemic insult to the brain or spinal cord. The spectrum includes monophasic, multiphasic, and progressive disorders, ranging from highly localized forms to multifocal or diffuse variants.[3] These different categories underscore the heterogeneous nature of demyelinating disorders, each with distinct mechanisms of injury, clinical manifestations, and prognostic implications.

Magnetic resonance imaging (MRI) is the imaging modality of choice to diagnose demyelinating disorders of the brain and spinal cord, as it provides unparalleled sensitivity in detecting white matter lesions and characterizing their distribution, morphology, and temporal evolution.[4] When interpreted in conjunction with clinical presentation and laboratory investigations, MRI not only aids in the early detection of demyelination but also allows accurate classification of the underlying disorder in most cases.

Treatment of demyelinating disorders depends on the underlying cause. Autoimmune conditions such as multiple sclerosis and neuromyelitis optica spectrum disorder often require long-term immunotherapy to reduce relapses and disease progression, while post-infectious syndromes like acute disseminated encephalomyelitis are usually managed with corticosteroids and, in resistant cases, immunoglobulin or plasmapheresis. For metabolic or hypoxic causes, management focuses on correcting the precipitating insult. Prognosis is variable, ranging from complete recovery in monophasic illnesses to chronic, disabling courses.

Despite the growing body of research on demyelinating disorders globally, data from low- and middle-income countries remain limited, particularly in South Asia. Variations in genetics, environmental exposures, and healthcare access may influence disease patterns, treatment responses, and long-term outcomes, underscoring the need for region-specific studies. The present study was therefore designed to investigate the spectrum of demyelinating disorders across multiple centers in Pakistan, with the aim of providing insights into their clinical characteristics and prognostic trends within this population.

METHODS

This was a multicenter cross-sectional observational study which was conducted between August 2017 and December 2019 across 39 neurology centers in Pakistan, representing public and private healthcare facilities in both urban and rural regions. All adults aged ≥18 years presenting to participating centers and diagnosed by trained neurologists were included. Ethics approval was obtained from the institutional review committees of participating centers. Written informed consent was obtained from all participants.

Diagnoses were made using standardized international criteria:

- Multiple sclerosis: 2017 McDonald criteria.
- NMOSD: 2015 International Panel for NMO Diagnosis (IPND) criteria.
- ADEM: Established clinical–radiological criteria.
- Leukodystrophies: Based on clinical presentation and MRI patterns suggestive of inherited white matter disorders. These were included as a small comparative subgroup due to initial presentation mimicking demyelinating disease.

Data included demographics, education status, comorbidities, and disability measured using the modified Rankin Scale (mRS).

Continuous variables were expressed as mean ± SD and categorical variables as frequencies and percentages. Univariate analyses were performed using independent t-tests and chi-square tests. Multivariable analysis was not undertaken due to the cross-sectional design, missing key covariates (disease duration, treatment exposure), and small subgroup sizes. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 373 patients with demyelinating disorders were analysed, including 151 males (40.5%) and 222 females (59.5%) with a mean age of 37.2 ± 11.7 years. Most patients were aged 31–45 years (38 %), followed by ≤30 years (35.1%), 46–65 years (23.6%), and >65 years (2.4%).

Education data were available for 70% of patients and findings were interpreted accordingly. Educational attainment varied significantly between genders (p=0.007). Overall, 18.8% were graduates or above, 22.0% had education below matric, and 18.5% were illiterate, while education status was undocumented in 30% of cases. Males were more likely to have completed graduation or higher education compared to females (26.5% vs. 13.5%), whereas illiteracy was more frequent among females (21.2% vs. 14.6%).

Age-related differences in education were also observed (p=0.13). Patients ≤30 years and 31–45 years had higher proportions of individuals educated at matric level or above (26.7% and 29.7%, respectively), while illiteracy was more frequent among older age groups (46–65 years: 14.8%; >65 years: 11.1%). In the oldest age group (>65 years), one-third were graduates, but this subgroup was very small (n=9).
Multiple sclerosis (MS) was the most frequent diagnosis (79.1%), followed by neuromyelitis optica (11.8%), acute disseminated encephalomyelitis (ADEM) (5.1%), and leukodystrophy (4.0%). MS was more prevalent among females (82.9% vs. 73.5%, p=0.02).

Comorbidities were observed in a subset of patients: hypertension in 9.4%, diabetes in 6.7%, and tobacco use in 2.7%. Diabetes was significantly more common among males (11.9% vs. 3.2%, p=0.001). Age-related differences were also significant: hypertension and diabetes were more frequent in older groups (p<0.001 and p=0.006).
With respect to disability, 33.5% of patients were fully functional, while 49.7% had minor disability without significant limitations. Moderate to severe disability was observed in 16.7%, including 9.9% requiring assistance with daily activities and 6.7% who were bedridden and dependent on constant care (Refer to Table 1). Disability was significantly more common in older age groups (p<0.001), as evident in Figure 1.

The autonomic nervous system (ANS), comprising of sympathetic and parasympathetic divisions, plays a vital role in regulating homeostasis through complex central and peripheral neural circuits that control visceral organ

Table 1: Percentage frequency of patients with grading of disability

Classification of Disability Status	Frequency	Percentage
Normal	125	33.5
Minor symptoms without disability, able to perform prior activities	101	27.1
Slightly disabled but can walk and do self care without assistance	58	15.5
Moderately disabled, needing some help but can walk unaided	26	7.0
Moderate to severe disability, unable to walk, needing some help in ADL	37	9.9
Severely disabled, bedridden, requiring constant care	25	6.7
Record not available	1	.3
Total	373	100.0

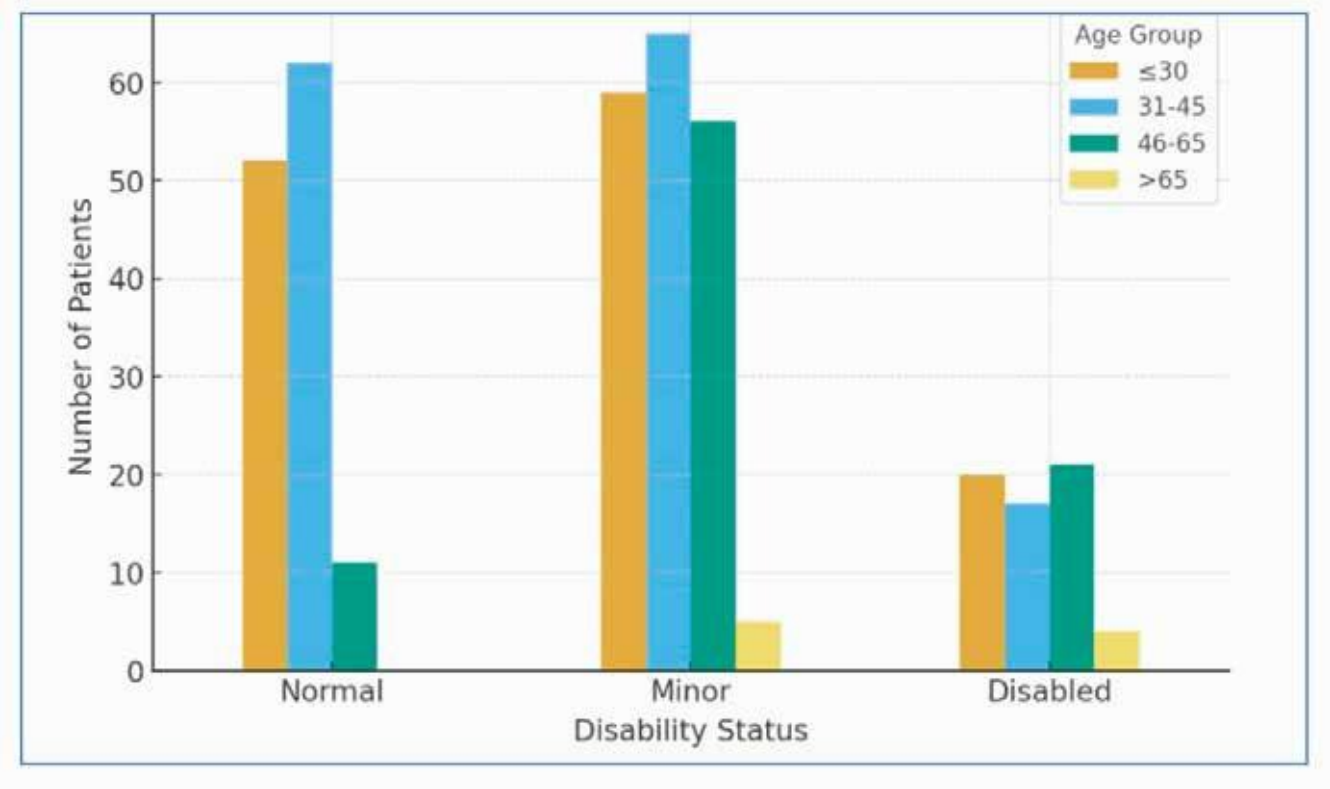

Figure 1: Status of Disability in demyelinating disorders as per specific age groups

DISCUSSION

This multicentre study provides the first comprehensive overview of demyelinating diseases in Pakistan, revealing important demographic and clinical patterns. MS was the most common diagnosis, followed by NMOSD, ADEM, and leukodystrophies. Female predominance, early adult onset, and substantial disability in a subset of patients align with global trends, yet the relatively higher burden of NMOSD and marked sociodemographic disparities highlight region-specific challenges.

The predominance of MS (79.1%) is consistent with global data showing MS as the leading demyelinating disorder.[5] The female preponderance observed parallels worldwide epidemiology, reflecting both biological and environmental risk factors.[6] Interestingly, NMOSD represented nearly 12% of cases, which is substantially higher than reports from Europe and North America (<5%) but comparable to East Asian and Middle Eastern cohorts.[7,8] These findings emphasizes the importance of accurate diagnostic differentiation in regional clinical practice.

Age distribution peaked in the 31–45-year group, the typical onset window for MS, but more than one-third of patients were ≤30 years.[9] Early disease onset in a young population may have long-term functional and socioeconomic implications, although longitudinal assessment is required to confirm this. The scarcity of patients >65 years likely reflects reduced survival of highly disabled patients and underdiagnosis in older adults.

Sociodemographic findings add further insight. Women were disproportionately represented among the illiterate and less educated groups, whereas men more often attained higher education. Given that education data were missing in nearly one-third of participants, these observations should be interpreted cautiously. Nonetheless, lower educational attainment has been associated with delayed diagnosis and poorer outcomes in MS in prior studies.

Comorbidities such as hypertension and diabetes were present in about 10% of patients, rising sharply with age. These rates are consistent with national surveys. Male patients had significantly higher rates of diabetes; a finding aligned with national trends.[10] The impact of these comorbidities on disability and disease course could not be evaluated in this study.

Although one-third of patients remained fully functional, nearly one in six had moderate-to-severe disability, including 6.7% who were bedridden. Disability increased with age, reflecting the cumulative burden of disease and

comorbidities.[11] These figures underscore the urgent need for early diagnosis and timely initiation of disease-modifying therapies, which can alter long-term outcomes.[12]

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