https://doi.org/10.56310/pjns.v17i01.172

MULTIPLE SCLEROSIS CARE IN PAKISTAN; ANALYSIS OF DATA PRESENTED AT FIRST PAKTRIMS CONFERENCE

Zara Shah[1], Haris Majid[2], Sadia Nishat[3], Sumera Rafat Umer[4], Sundus Mehtab Shafee[4], Ahmed Wali[5], Naila Shahbaz[4], Mughis Sheerani[3], Mohammad Wasay[1]

[1]Aga Khan University, Karachi
[2]Pakistan Institute of Medical Sciences, Islamabad
[3]Sindh Institute of Urology and Transplantation, Karachi
[4]Dow University of Health Sciences, Karachi
[5]Bolan Medical complex, Quetta

Correspondence Author: Zara Shah (MBBS) *Section of Neurosurgery, Department of Surgery, Aga Khan University Hospital, Karachi* ***Email:*** *zarashah97@gmail.com*

Date of submission: *May 1, 2022* ***Date of revision:*** *September 8, 2022* ***Date of acceptance:*** *October 6, 2022*

ABSTRACT

Novel data on Multiple Sclerosis (MS) in Pakistan from leading institutes in the country was presented at the first Pakistan Treatment in Multiple Sclerosis (PAKTRIMS) Conference, organized by the section of Neurology, department of Medicine, Aga Khan University, Karachi on Saturday, December 18, 2021. Pakistan has been considered to have a low prevalence of MS; however, recent research reveals that it is not as uncommon as previously believed to be in the country. The true prevalence and incidence of MS in the country is unknown because of dearth of research. Data of MS patients enrolled in various private and public institutes in Pakistan highlights the current treatment offered in Pakistan for MS patients with steroids as the mainstay treatment and disease modifying therapy (DMT) mainly including azathioprine, ocrelizumab and rituximab. Available data featuring disease progression indicates a successful response to the treatment offered to patients with improved expanded disability status scale (EDSS) and radiological findings. The conference was a stepping stone towards future research in Pakistan as it has highlighted further requirements in the field of MS as far as our country is concerned. Available data majorly outlines demographic and disease characteristics, however, there is a need for research to fill in the gap for data in reporting MS diagnosis, treatment, and disease outcome to develop a better healthcare system geared towards MS patients in a low- and middle-income Country (LMIC).

KEYWORDS: Multiple sclerosis; Pakistan; Treatment; Conference

INTRODUCTION

Multiple Sclerosis (MS) is an inflammatory disease of the central nervous system (CNS) which presents with an array of symptom.[1] The disease affects an estimated 2.8 million people worldwide.[2] Although Pakistan has been considered a low prevalence country, current research suggests MS may be more common than previously thought.[3] In Pakistan, a low- and middle-income country (LMIC), the prevalence of MS is approximately 10 per 100000 people. The previously considered low prevalence could be due to lack of awareness, unavailability of doctors or lack of diagnostic resources.[4] Research is currently being carried out in the hopes of successfully bridging the gap between MS patients and their access to health care in the country.[5] Although existing literature highlights steroids as the mainstay treatment offered in Pakistan; disease modifying therapies (DMTs) including mitoxantrone, rituximab, beta-interferon, methotrexate, azathioprine, cyclophosphamide, teriflunomide, leflunomide, alemtuzumab, ocrelizumab, natalizumab and fingolimod are currently available and offered for MS management in Pakistan.[4] To address the future of MS in Pakistan the first Pakistan Treatment in Multiple Sclerosis (PAKTRIMS) Conference was held on Saturday, December 18, 2021. It was organized by the section of Neurology, department of Medicine, Aga Khan University, Karachi. Leading neurologists from across the country attended the conference and novel data was presented on adult and pediatric MS patients from various parts of the country. Neurologists presented data from Pakistan's topmost public secondary and tertiary hospitals which included Sindh Institute of Urology & Transplantation (SIUT), Dr. Ruth K. M. Pfau Civil Hospital karachi, Pakistan Institute of Medical Sciences (PIMS), Sheikh Khalifah Bin Zayyad Hospital and Bolan Medical Complex Hospital. Data of patients enrolled at the leading private secondary and tertiary hospitals of Pakistan; Aga Khan University Hospital and Sultan Tareen Hospital, was also presented. The conference was a stepping stone towards the future of MS in Pakistan. A summary of the data presented from different institutes is summarized in Table 1.

Aga Khan University Hospital, Karachi

A retrospective review was conducted at the Department of Medicine at the Aga Khan University Hospital in Karachi Pakistan from December 2019 to September 2020. Medical records of all adult patients aged 18 years and above presenting with MS according to the McDonald's criteria were included (6).[6] This review presents one of the largest study samples to date of Multiple Sclerosis patients in Pakistan highlighting demographic characteristics, disease characteristics, readmission causes and treatment options. A total of 163 patients were selected. Relapsing remitting MS was the most common type of MS found in the patients (91.4%) followed by primary progressive MS (4.9%) and secondary progressive MS (3.7%). Unlike previous studies, this study describes MRI (Magnetic Resonance Images) findings in detail. The most common finding on T2 or flair MRI scan was presence of lesions in multiple foci found in 62.0% cases, with similar findings found in 17.1% cases on Gadolinium-enhancing MRI. Multiple foci were most seen in the periventricular region (44.8%) followed by the juxta-cortical region (43.6%). Data was collected on past and present treatment received by the patients. Patients had commonly been prescribed with oral and intravenous steroids (55.8%, 43.6%) and azathioprine was found to be the most common disease modifying therapy (DMT) prescribed in the past (30.7%). Rituximab (3.1%), per oral steroids (1.2%), beta interferon 1A (1.2%), and azathioprine (1.2%) were the most common treatments prescribed as current management. The most common disease complication highlighted by this study is MS exacerbation which occurred in 8.6% of the patients. This study has limitations in the data collected as it does not include disease progression with treatment however its strengths lie in its extensive data collection related to some neglected aspects of MS epidemiology, MRI features and management in Pakistan.

Pakistan Institute of Medical Sciences, Islamabad

An extensive review was carried out on CNS demyelinating diseases from January 2017 till December 2021 at Pakistan Institute of Medical Sciences, Islamabad (PIMS). The study was done retrospectively as well as prospectively during this time. Patients diagnosed with MS according to the McDonald's criteria and 12 years and older were included (6). Other CNS demyelinating disorders included in this study were clinically isolated syndrome (CIS), neuromyelitis Optica spectrum disorders (NMOSD) and Acute disseminated encephalomyelitis (ADEM). 142 patients of MS were included in the study. The most common disease course seen was relapsing remitting MS (74.6%) followed by primary progressive MS (15.5%). The study presented the treatment offered to patients presenting with CNS demyelinating diseases. Rituximab was prescribed to 9.2% patients with MS out of which 30.8% of the patients had been switched to ocrelizumab. Treatment for MS patients also included azathioprine (1.4%) and plasmapheresis (2.1%). This review offers voluminous data centering around CNS demyelinating diseases and disease progression with treatment; however, it has a few limitations as it did not include complications related to MS or radiological findings of these patients.

Sindh Institute of Urology & Transplantation (SIUT), Karachi

Rituximab is a monoclonal antibody which is widely administered off label for MS treatment as it is well tolerated and has a favorable cost effectiveness profil.[7] There is ongoing data collection since 2017 of patients diagnosed with MS presenting to Sindh Institute of Urology & Transplantation (SIUT), Karachi. To date, there are 55 patients with MS with their age ranging from 18 to 55. All patients have been treated with rituximab. The maximum number of doses of rituximab given to a patient is 8. This DMT has shown encouraging disease outcomes in this population for example one patient's expanded disability status scale (EDSS) has improved from 4.5 to 2 since the start of treatment with rituximab. The current data presented has limitations as it does not include patient demographics, disease progression and MRI findings however it does highlight the vital role played by rituximab in patients with MS in Pakistan.

Dr. Ruth K. M. Pfau Civil Hospital, Karachi

Data was collected from July 2018 till June 2021 on patients presenting with demyelinating diseases to the neurology department of Dr. Ruth K. M. Pfau Civil Hospital, Karachi. Patients were diagnosed with either MS, CIS or NMOSD. 27 patients were diagnosed with MS. The age of the patients varied from 14 to 49 with a median age of 26. The most common clinical presentation was cranio-optico-spinal (26%) followed by cranio-spinal (22%). Relapsing remitting MS was the most common type of MS (67%) followed by primary progressive MS (22%). Patients were prescribed azathioprine (44.4%), mitoxantrone (37.0%), ocrelizumab (14.8%) and cyclophosphamide (3.7%). All patients presenting with acute presentation of MS were administered with pulse steroids. Disease progression was measured in patients who had been prescribed with treatment for at least 6 months.

Considering radiological representation of the disease and EDSS, 55% of the patients showed improvement in disease progression whereas 15% of the patients deteriorated including one death due to drug induced neutropenic sepsis. 30% of the patients showed no change in the course of the disease after a minimum of 6 months of treatment. Although the study presents a small cohort, it extensively presents data on disease presentation and treatment outcome.

Sheikh Khalifah Bin Zayyad Hospital, Bolan Medical Complex Hospital, Sultan Tareen Hospital, Quetta

Ocrelizumab is a Food and Drug Administration (FDA) approved monoclonal antibody for MS. It is generally well tolerated and highly efficacious DMT.[8] A prospective study is being carried out on patients diagnosed with MS presenting to three hospitals in Quetta including Sheikh Khalifah Bin Zayyad Hospital, Bolan Medical Complex Hospital and Sultan Tareen Hospital. The objective of this study is to assess the efficacy and disease progression in patients with MS receiving ocrelizumab. Patients diagnosed with MS aged 16 years and older are included in the study. There are currently 9 patients of MS included in the study with relapsing remitting MS as the most common type of presentation (89%). Paraparesis has been the most common symptom (44%) followed by visual impairment (33.3%), sensory impairment (33.3%) and ataxia (33.3%). MRI of the brain and spinal cord represents typical findings of MS in 78% of the patients. All patients are given two doses of 300mg of ocrelizumab, 14 days apart followed by a 600 mg dose after 6 months. Patients are then given subsequent doses every 6 months. Patients are evaluated before receiving treatment and then three, 6 and 12 months after the initiation of treatment. Their clinical status is measured by EDSS. The median EDSS before receiving ocrelizumab is 7.5 compared to a median score of 4 after a year of treatment. No significant adverse effects have been reported however two patients have complained of nausea while receiving treatment. This ongoing study provides immense information on ocrelizumab as a treatment for patients with MS in Pakistan. Although the study sample is comparatively low, new patients are currently being enrolled into the study including 6 patients who have already received their first dose of ocrelizumab.

Table 1: Summary of data presented

Institute	Number of Patients	Treatment Offered	Outcome
Aga Khan University Hospital, Karachi	163	• Alemtuzumab • Azathioprine • IVIG • IM/IV/PO Steroids • Beta interferon 1A • Beta interferon 1B • Fingolimod • Mitoxantrone • Methotrexate • Ocrelizumab • Plasmapheresis • Rituximab	
Pakistan Institute of Medical Sciences, Islamabad	142	• Azathioprine • Ocrelizumab • Plasmapheresis • Rituximab	
Sindh Institute of Urology & Transplantation, Karachi	55	• Rituximab	1 patient: Pre rituximab EDSS 4.5 to post rituximab EDSS 2.
Dr Ruth K. M. Pfau Civil Hospital, Karachi	27	• Azathioprine • Cyclophosphamide • Methylprednisolone • Mitoxantrone • Ocrelizumab	Improved:15 Worsened:3 Static:8
Sheikh Khalifah Bin Zayyad Hospital, BolanMedicalComplex Hospital, Sultan Tareen Hospital, Quetta	9	• Ocrelizumab	Median EDSS before Ocrelizumab: 7.5 Median EDSS on 12 month follow up: 4
MS: Multiple Sclerosis EDSS: Expanded Disability Status Scale			

CONCLUSION

New research is exploring the characteristics of MS in Pakistan with increased focus on treatment and outcome of the disease in the country. It is unveiling the barriers to disease diagnosis and management in the country. However, there is no population-based study to determine the prevalence or incidence of MS in Pakistan. The PAKTRIMS conference was able to set the stage for the announcement of the launch of the Multiple Sclerosis Pakistan Registry which is an online application-based registry, compatible with android and iOS and aims to collect data of one thousand MS patients across the country in the span of one year. This will hopefully present a clearer picture of the disease in the country.

REFERENCES

1. Doshi A, Chataway J. Multiple sclerosis, a treatable disease. Clin Med (Lond). 2016;16(Suppl 6):s53-s9.
2. The Lancet N. Multiple sclerosis under the spotlight. Lancet Neurol. 2021;20(7):497.
3. Wasay M, Ali S, Khatri IA, Hassan A, Asif M, Zakiullah N, et al. Multiple sclerosis in Pakistan. Mult Scler. 2007;13(5):668-9.
4. Shah Z, Wasay M, Chaudhry BZ, Fredrikson S. Multiple sclerosis in Pakistan: Current status and future perspective. J Neurol Sci. 2020;418:117066.
5. Syed MJ, Shah Z, Awan S, Wasay M, Fredrikson S. Telephone validation of an Urdu translated version of the extended disability severity scale in multiple sclerosis patients. Mult Scler Relat Disord. 2021;48:102684.
6. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162-73.
7. Chisari CG, Sgarlata E, Arena S, Toscano S, Luca M, Patti F. Rituximab for the treatment of multiple sclerosis: a review. J Neurol. 2022;269(1):159-83.
8. Lamb YN. Ocrelizumab: A Review in Multiple Sclerosis. Drugs. 2022;82(3):323-34.

Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil