

Challenges to multiple sclerosis care in Pakistan

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Multiple sclerosis (MS) is the commonest cause of non-traumatic neurological disability in the young population.¹ It is an immune mediated disorder affecting the central nervous system.² Improvements in diagnostic modalities and formalization of diagnostic criteria have led to earlier and accurate diagnosis. Pakistan is amongst the low prevalence region for Multiple sclerosis.³ The estimated prevalence reported is at 10 per 100,000 persons to be suffering from MS.⁴ There is however increasing evidence that the south Asian region MS prevalence is underestimated, as reported in several studies from our neighbouring country Iran.⁵

As is the case with most neurological disorders, there are no population based studies, and no data for Multiple sclerosis at the national database level is available.³ MS research in Pakistan is limited to mostly case reports, only a few case series have been published. Different aspects of disease impact have not been reviewed. Resource utilization and diagnostic issues also have not been discussed.³ The biggest study published till date consists of multicentre data collected from Pakistan Institute of Medical Sciences, Islamabad, and Aga Khan University Hospital, Karachi comprising of 188 patients.⁴ More than 1000 cases of MS and related disorders are published from various centres in Pakistan.⁶⁻²² A list of all major case series published till date from various centres of Pakistan is provided in the appendix.

There has been no study directly discussing the diagnostic challenges in MS. Obvious factors include, but are not limited to, small number of neurologists, lack of awareness with diagnostic criteria on part of both radiologists and neurologists. Non-standardised reporting's of neuroimaging and lower strength MRIs used in evaluation of patients due to non-availability of higher strength MRI machines. Interestingly there has been work done on genetics of MS in Pakistan, which was done in collaboration with Karolinska Institute of Sweden.²³ The study compared the prevalence of HLA haplotypes between patient and control groups and its

correlation with disease severity. The study showed no statistically significant difference between the MS patients and control groups. However, there was a strong association between high Expanded Disability Status Scale (EDSS) score (>6) and DQB1*0203 haplotype ($p=0.04$).²³ MS related disability assessment and its management is yet another big challenge. Number of properly trained physical medicine and rehabilitation (PM&R) physicians available is limited. The number of qualified PM&R physicians in entire Pakistan is still under fifty. EDSS is a validated tool for assessing functional disability in MS. A local study assessed telephonic validation of translated version in Urdu of telephonic EDSS.²⁴ There was a high concordance rate found between in person EDSS and telephonic EDSS.

Availability of MS drugs is a serious limitation in offering therapy to patients. So far only 5 FDA (food and drug administration, USA) approved disease modifying MS therapies are available in Pakistan. These include Interferon Beta-1b (Sub cutaneous injection), Ocrelizumab (Infusions), Teriflunomide (per-oral tablets), Alemtuzumab (infusion) and Mitoxantrone (infusion). Off label medication usage is not uncommon. The main factor for usage is the significant cost difference when compared with approved medications. These include Azathioprine (oral tablets), Leflunomide (oral tablets), Cyclophosphamide (infusion), Rituximab (infusion) and Methylprednisolone (monthly infusions). Cost is an

Table-1: Mean organ weights (g) and ventricle thicknesses (cm) of the study population.

Name	Approximate Cost in Pakistan rupees	Annual Cost in Pakistan Rupees
1. Interferon Beta-1b (300mcg)	70,000 Rs for 15 vials	8,40,000 Rs
2. Ocrelizumab (300mg)	4,40,000 Rs for 2 vials	8,80,000 Rs
3. Teriflunomide (14mg)	92,600 Rs for 28 tablets	11,112,00 Rs
4. Alemtuzumab (12mg)	15,00,000 Rs for 1 injection	75,00,000 Rs
5. Mitoxantrone (12mg)	4,000 Rs for 1 vial	20,000 Rs
6. Azathioprine (50mg)	15 Rs tablets	16,200 Rs
7. Leflunomide (20mg)	49 Rs per tablet	17,640 Rs
8. Cyclophosphamide (500mg)	138 Rs for 1 vial	2,484 Rs
9. Rituximab (500mg)	72,675 Rs for 1 vial	2,90,700 Rs
10. Rituximab biosimilars (500mg)	40,000 Rs for 1 vial	1,60,000 Rs
11. Methylprednisolone (1000mg)	4,210.65 Rs for 1 vial	50,527.8 Rs

Note: The costs mentioned are mostly retail prices and may vary amongst different pharmacies and brands or generics.

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Appendix: List of published manuscripts from Pakistan

First Author	Year of Publication	Method	Study setting	Diagnostic criteria used	Number of Cases	Female: Male ratio	Mean age of onset (years)
Raza SQ ⁶	1998	Retrospective	Hospital based	-	25	1.5:1	27.8
Siddiqui I ⁷	2002	Retrospective	Single center, Aga Khan University Hospital, Karachi	-	15	-	-
Wasay M ⁸	2007	Retrospective	Multicenter, hospital based	Poser criteria, Thompson criteria	142	1.45:1	27
Shahwar H ⁹	2008	Prospective	Single center, Jinnah Post Graduate Medical Center, Karachi	Poser's criteria	20	2:1	25.8
Kazim SF ¹⁰	2010	Retrospective	Single center, hospital based	-	46	2.5:1	-
Saleem K ¹¹	2011	Prospective	Single center, Mayo Hospital, Lahore	-	30	1.30:1	-
Khatri IA ¹²	2012	Retrospective	Single center, Shifa International Hospital, Islamabad	-	24	1.66:1	-
Javid MA ¹³	2012	Prospective	Multicenter, hospital based	2010 Revised McDonald criteria	64	1.56:1	36
Wasay M ¹⁴	2013	Prospective	Multicenter, hospital based	-	100	1.5:1	-
Ahmad A ¹⁵	2013	Prospective	Single center, Shifa International Hospital, Islamabad	-	4	3:1	27.7
Zaidi NR ¹⁶	2014	-	Single center, Mayo Hospital, Lahore	-	30	1:1	-
Javed MA ¹⁷	2014	Retrospective	Single center, Mayo Hospital, Lahore	2010 Revised McDonald criteria	23	1.09:1	29.5
Ali A ¹⁸	2017	Prospective	Single center, Jinnah Post Graduate Medical Center, Karachi	-	85	1:1.07	-
Javid MA ¹⁹	2017	Retrospective	Multicenter, hospital based	2010 Revised McDonald criteria	15 (pediatric patients)	1.5:1	-
Pechuho SJ ²⁰	2018	Prospective	Single center, Chandka Medical College Hospital, Larkana	2010 Revised McDonald criteria	85	1.36:1	-
Hikmatullah KS ²¹	2021	Prospective	Single center, Pak-Emirates Military Hospital Rawalpindi, Rawalpindi	2010 Revised McDonald criteria	54	-	31.93
Zarah S ⁴	2022	Retrospective	Multicenter, Pakistan Institute of Medical Sciences, Islamabad, Aga Khan University Hospital, Karachi	2017 Revised McDonald criteria	188	1.68:1	31.1
Mehwish AB ²²	2022	Prospective	Single center, Civil Hospital, Karachi	2017 Revised McDonald criteria	165	1.60:1	32.92

important determinant for use in disease. Approximate cost of available medications is provided in table 1. As can be appreciated from the table, the cost of approved medications is extremely high, and it is not possible for most of the patient population to initiate or continue treatment for a long time.

There are certain financial support programmes available in several countries including Pakistan's Baitul Maal (PBM), Ehsas tahafuz programme and Chief minister fund. Pakistan Baitul Maal (PBM) is one of the oldest government financial assistance programmes for diseased patients. It is operational and working in most

government hospitals. Its limitations include the financial support provided which is up to a maximum of 600,000 rupees. This is not a viable option in chronic diseases like multiple sclerosis where the duration of therapy in most cases is expected to be for several decades. PBM financial assistance is limited to patients presenting to government hospitals. Ehsas tahafuz programme, is another unique financial assistance programme from which several patients of multiple sclerosis are benefitting. Its limitations are that its availability is so far only in the provinces of Khyber Pakhtunkhwa and Baluchistan. Very few hospitals in Punjab are registered with this programme. This is also exclusively for

government sector hospitals. Chief minister fund is a programme so far functional only in the province of Punjab. They are again only providing services in designated government hospitals. Non-governmental organizations (NGOs) and government's financial assistance programme can be up scaled and directed to play a more effective role in patient's care for multiple sclerosis. This is one of the main sectors which requires special emphasis for more equal distribution of MS care.

A comprehensive multipronged strategy is required to organize and improve MS care in Pakistan. The total number of neurologists registered in Pakistan till date (Jan 2023) is under 350 in total (213 have done FCPS neurology, the remaining are either foreign qualified or have done MD or DCN in Neurology). Based on the estimated prevalence of MS in Pakistan of 10 per 100,000 population, the number of trained neurologists is too low to cater to the mounting number of MS patients.⁴ Even the trained neurologists have limitation because of lack of availability of diagnostic tools or inexperience in dealing with MS patients. This poses a significant capacity building challenge for training neurologists, medical specialists and PM&R physicians in dealing with Multiple sclerosis patients.

In order to cater to the need of capacity building, two forums have been created for MS education and research. The first one is MS research and education forum (MSREF). The MSREF has conducted one day training workshops in 2019 in 5 major cities of Pakistan, Karachi, Islamabad, Multan, Quetta, and Peshawar. A comprehensive curriculum covering the diagnostic and treatment aspects of MS was covered in these workshops with the engagement of speakers from respective cities. The target audience includes Neurologists, Medical specialists, Radiologists, Ophthalmologists, PM&R physicians, and neurosurgeons. The workshops were duly accredited and CME certification was also awarded. Since 2021, Aga Khan university along with MSREF started PAKTRIMS i.e., Pakistan committee for treatment and research in Multiple Sclerosis. The first conference was a virtual event held in December 2020. A report regarding the conference was recently published.²⁵ The second conference was held on 20th December 2022 in Islamabad in hybrid format within person and virtual audience. Multiple national and international speakers participated. In addition to disease related talks, a session was conducted regarding disease presentation in different cities of Pakistan. The Second PAKTRIMS annual conference has also played a role in imparting MS education. The pharmaceutical industry and financial assistance programmes also need to be aligned to

provide solutions which are workable and can lead to provision uninterrupted medications, specifically disease modifying therapies to the patients. A major step towards this effort was undertaken in the 2nd PAKTRIMS where industry representatives and directors of financial assistance programmes participated. However further work is needed in this area. Lastly, one area which can be developed with little financial impact is MS data collection.³ A registry in this respect has been established, but so far there has been little contribution as far as data collection is concerned. If the government can officiate a mandatory national MS database, requiring mandatory patient registration MS research, education and patient care can improve dramatically and more effective planning can be devised

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