Original Article

Study to Compare the Efficacy and Cost-Effectiveness of Various Disease Modifying Drugs in the Management of Multiple Sclerosis in India- An Observational Study

Mukul Sehrawat[1,2], Santhosh K. Madhusudhan[1,2], Shubha D. Bakkappa[3,2], Srinivas L. Devendrappa[1,2]

Departments of [1]Pharmacology and [3]Community Medicine, [2]JJM Medical College, Davangere, Karnataka, India

Abstract

Background: Real-world data on the efficacy and cost-effectiveness of multiple sclerosis (MS) disease-modifying drugs (DMTs) is lacking in the Indian setting. The primary objective of this study was to evaluate the efficacy of DMTs, and the secondary objective was to evaluate cost-effectiveness and the quality of life (QoL) in these patients. **Method:** Seventy-four patients fulfilling study criteria were recruited in the retrospective observational study, of which 69 completed the study. Primary outcome was measured by annualized relapse rate (ARR), and secondary outcome was measured by WHOQOL-BREF scale, modified Kuppuswamy scale, and rating of DMT scale through a subjective questionnaire. **Results:** Patients on natalizumab, rituximab, and glatiramer acetate showed the highest reduction in ARR. The highest reduction of ARR (2.5) was produced by natalizumab and least by Peg-IFNβ1a (0.5). In QoL analysis, teriflunomide group had the highest average score for both physical health (22.7, SD 4.7) and psychological (21.3, SD 4.0) domains, whereas natalizumab group had the lowest average score. Socio-economic status analysis showed DMF, IFNβ 1a, peg-IFNβ 1a, rituximab, and glatiramer acetate are affordable to the upper middle class and above, whereas natalizumab could be afforded only by high-class strata. Teriflunomide was most affordable annually. Study of adverse drug reactions showed natalizumab was very well tolerated by the study participants. **Conclusion:** Natalizumab, an infusion DMT, was highly effective in terms of reducing the ARR. Rituximab, an off-label DMT, was found to be very effective. Teriflunomide was overall an effective DMT in terms of affordability, QoL balance, and an acceptable ARR reduction.

Keywords: Annualized relapse rate, cost-effectiveness, disease modifying therapies (DMT), multiple sclerosis, quality of life

Introduction

Inflammation brought on by the autoimmune disease multiple sclerosis (MS) results in demyelination and neurodegenerative alterations in the central nervous system.[1] It is the most frequent cause of non-traumatic impairment, which raises the morbidity rate in young people.[2] According to the Atlas of MS Epidemiology study, it is estimated that the number of individuals with MS in India could range from 1,00,000 to 2,00,000.[3] However, the actual number could be higher as a result of limited epidemiological data, diagnostic resources, and a shortage of neurologists, thus highlighting it as a burgeoning neurological concern in the Indian context. In MS, chronic demyelination along with the degenerative autoimmune reaction cause focal inflammation leading to neuronal death. This disruption leads to a range of MS symptoms, neurological deficits, and disability.[4] The slowing of signal conduction or blocked signals can lead to muscle weakness, imbalance, tingling sensations, dizziness, fatigue, difficulty in movements, muscular in-coordination, vision problems, strength, and sensation issues. Early diagnosis and initiation of Disease Modifying Drugs or Therapies (DMDs/DMTs) in MS patients can prevent acute relapses, disease progression, and disability. Various DMDs have been developed over the years, with initially the introduction of interferons followed later by glatiramer acetate, both administered as intramuscular injections, and then came natalizumab, administered by intravenous route. These drugs were followed by oral preparations like dimethyl fumarate (DMF), fingolimod, and teriflunomide which have the advantage of better compliance and are cheaper than injectables. All these DMDs are available in India in both branded and biosimilar forms, except for natalizumab and pegylated interferon beta 1a, which are available only under the brand names Tysabri and Plegridy, respectively.[4] The DMT therapy in MS can last for a very long period if not spanning the remaining lifetime of the patient. Pharmacoeconomic studies have highlighted the importance and need for cost-effectiveness, cost-benefit, and cost-utility studies in MS patients.[5] Such studies enable physicians to choose and provide better-suited treatment to patients. These studies

Address for correspondence: Dr. Mukul Sehrawat, H. No. 2917, 5th Main, 2nd Cross, MCC B Block, Davangere - 577 004, Karnataka, India.
E-mail: mukulsehrawat22@gmail.com

Submitted: 26-May-2023 **Revised:** 03-Aug-2023 **Accepted:** 08-Aug-2023
Published: 27-Sep-2023

DOI: 10.4103/aian.aian_467_23

also provide a measure of the cost incurred by the families of the patient and the burden of the disease on the healthcare system, thus forming the baseline for policy-making. In India, with less than 40% Health insurance coverage and more than 65% of the population incurring catastrophic Out-of-Pocket expenditure for Health services each year,[6] the cost of therapy in one way or another becomes a very relevant factor. The recent introduction of various DMDs in the Indian market has created a knowledge gap on the cost-effectiveness of these drugs in Indian patients. This study sought to retrospectively analyze the cost-effectiveness of several DMDs offered the Indian market. This study's primary goal was to produce and compare real-world data on the cost-effectiveness of DMDs in the treatment of relapsing-remitting MS, and its secondary goal was to evaluate the quality of life (QoL), socio-economic status, and adverse drug reactions in these patients.

Study method

This retrospective observational study was carried out in 2 months between June 2021 and July 2021. Participants were enrolled as per the inclusion criteria of the study. Patients of any age diagnosed with Relapsing-Remitting Multiple Sclerosis (RRMS) as per McDonald's criteria,[7] with treatment data available for 1 year prior and 1 year post the index date, were included. Exclusions were pregnant/lactating women, non-consenting patients, and those with co-morbidities/chronic diseases impacting the QoL. In light of the limited prevalence of MS in India and the institutional requirement of a 2-month study duration, an arbitrary study sample of 75 was decided.

Data collection

MS patients were contacted through a patient welfare society, and those who met the study criteria and provided informed consent were enrolled. A pretested questionnaire was used to obtain demographic information. Each participant was individually interviewed for obtaining the rest of the information pertinent to the study. Considering participant safety during the prevailing period of COVID-19 and convenience, the interviews were carried out using video teleconferencing. The study was approved by the institutional ethical committee and confidentiality was ensured as per National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017)[8] and the Helsinki Declaration of 1964 (revised October 2013).

Primary outcome measures

Annualized relapse rate (ARR)[9] was used for efficacy assessment. It was calculated by dividing total relapses per period by person-years. Pre-index ARR was used as the disease severity baseline before the initiation of the DMTs. ARR reduction has been categorized as high (≥91%), moderate (50–90%), or low (<50%).

Secondary outcome measures

QoL and socioeconomic status were assessed through WHOQOL-BREF[10] and the modified Kuppuswamy socioeconomic scale[11] (MKSS), respectively. Rating of DMT (ROD) is a subjective rating of the participant's experience with DMT, covering aspects like availability, affordability, efficacy, ease of administration, and impact on QoL. Each domain of ROD was graded on a scale of 1–10 based on participant experience, and an average of these domain scores represents the overall ROD.

For data analysis, Microsoft Excel software was used. Due to the sample size and study duration restraints, statistical analysis was deferred for this study. For any missing data, participants were followed up with a second interview, and as for non-completions, participant data was removed from the study in its entirety.

Results

Seventy-six individuals with RRMS were screened for the study. After checking for eligibility, 74 patients were enrolled in the study. Out of the 74 participants, 69 (93.2%) completed the study. Out of 69 patients who completed the study, 37.7% had initiated treatment with DMF, 17.4% with teriflunomide, 24.6% with interferon beta-1a (IFNβ 1a), 5.8% with pegylated interferon beta-1a (Peg IFNβ 1a), 4.4% with glatiramer acetate (GA), 5.2% with rituximab, and 2.9% with natalizumab.

Baseline characteristics

62.3% of participants in the study were females, with a mean age at DMT initiation ranging from 27.6 years in the rituximab group to 34.8 years in the IFNβ 1a group. The baseline demographics of patients are given in Table 1. Nearly half the study participants used branded DMTs whereas 49.3% used biosimilars. As for geographical distribution, the majority of participants were from south India (49.2%) with the least from central India (1.4%). The marital status of study participants was assessed in three categories, that is, married, previously married, and never married. More than 50% of participants in every group were never married except for patients initiated with GA and IFNβ 1a. All study participants had attained formal schooling. More than 50% of the participants were graduates in every DMT group with the highest share of graduates in the teriflunomide (91.7%) group and the lowest share of graduates in natalizumab and Peg-IFNβ 1a groups at 50%. Participants in the GA group had the highest average duration of disease at 11.0 years, and the lowest average duration of disease was seen in the DMF group at 5.3 years.

Annualized relapse rate (ARR)

Pre-DMT and post-DMT ARR were calculated for each group. Using pre-index ARR as a marker for disease severity before initiating DMT and assessing its reduction demonstrates the pharmacological efficacy of DMTs. Pre-index ARR ranged from the lowest of 0.7 for GA to the highest of 2.5 for Natalizumab. The highest ARR reductions of 100% were produced by natalizumab (2.5), rituximab (1.8), and GA (0.7), whereas peg-IFNβ 1a had the lowest at 0.5 (50%). While both GA and natalizumab showed a 100% ARR reduction, the difference in their pre-index ARR values indicates that

natalizumab effectively managed a more aggressive disease compared to GA. Oral DMTs like DMF and teriflunomide had a moderate ARR reduction of 0.7 (58.8%) and 1.0 (77.4%), respectively. Another injectable DMT, IFNβ 1a had an ARR reduction of 1.0 (71.9%) [Table 2].

Quality of life

The WHOQOL-BREF scale, which has 26 items and evaluates four domains—physical health, psychological health, social interactions, and the environment—was used to measure QoL. The study found significant variation in WHOQOL-BREF domain-wise average scores among different groups. The teriflunomide group showed the highest average scores for both the physical health domain (22.7, SD 4.7) and psychological domain (21.3, SD 4.0), while the natalizumab group showed the lowest average scores for both domains (14.5, SD 10.6 and 15, SD 12.7, respectively). In the social relationships domain, the natalizumab group had the highest average score (12.0, SD 2.8), while interferon beta-1a had the lowest average score (9.2, SD 2.4). In the environment domain, glatiramer acetate had the highest average score (29.00, SD 5.3), while rituximab had the lowest average score (25.3, SD 4.1) [Table 3].

Table 1: Baseline demographics of study participants

Drug Group→ Variables ↓	DMF*	TFM†	IFNβ 1a	Peg-IFNβ 1a	GA‡	RTX§	NTZ‖
Participant Count (n)	26	12	17	4	3	5	2
Age at index date, mean (SD)	33 (8.80)	33.08 (8.911)	34.76 (8.01)	32.75 (8.25)	33.33 (11.44)	27.6 (6.15)	29 (9.00)
Female %	46.2	66.7	70.6	50.0	100.0	80.0	50.0
Male%	53.9	33.3	29.5	50.0	0.0	20.0	50.0
DMT type %							
Brand Name	46.2	16.7	82.4	100.0	0.0	40.0	100.0
Biosimilars	53.8	83.3	17.6	0.0	100.0	60.0	0.0
Region%							
Northern India	15.4	16.7	17.6	25.0	0.0	40.0	0.0
Eastern India	15.4	0.0	11.8	0.0	0.0	0.0	50.0
Western India	30.8	25.0	0.0	50.0	0.0	40.0	0.0
Central India	0.0	0.0	5.9	0.0	0.0	0.0	0.0
Southern India	38.5	58.3	64.7	25.0	100.0	20.0	50.0
Marital status%							
Married	38.5	33.3	35.3	0.0	66.7	0.0	50.0
Previously married	7.7	16.7	29.4	50.0	33.3	20.0	0.0
Never married	53.8	50.0	35.3	50.0	0.0	80.0	50.0
Education%							
10th	0.0	8.3	5.9	25.0	0.0	0.0	0.0
12th	0.0	0.0	5.9	0.0	0.0	0.0	0.0
Graduation	69.2	91.7	70.6	50.0	100.0	80.0	50.0
Post-graduation	30.8	0.0	17.6	25.0	0.0	20.0	50.0
Average Duration of Disease in Years (SD)	5.3 (3.8)	6.4 (5.1)	9.7 (3.8)	7.8 (4.3)	11.0 (4.4)	9.5 (10.6)	7.0 (7.7)

*Dimethyl fumarate, †Teriflunomide, ‡Glatiramer acetate, §Rituximab, ‖Natalizumab

Table 2: Efficacy evaluation of DMTs based on ARR

Efficacy Analysis	DMF	TFM	IFNβ 1a	Peg-IFNβ 1a	GA	RTX	NTZ
Relapses in the Year before %							
0	23.1	25.0	5.9	25.0	33.3	20.0	0.0
1	38.5	50.0	52.9	50.0	66.7	40.0	0.0
≥2	34.6	25.0	41.2	25.0	0.0	40.0	100.0
Pre-index ARR	1.2	1.3	1.4	1.0	0.7	1.8	2.5
Relapses in the Year after %							
0	53.8	75.0	76.5	50.0	100.0	100.0	100.0
1	42.3	16.7	11.8	50.0	0.0	0.0	0.0
≥2	3.8	8.3	11.8	0.0	0.0	0.0	0.0
Post-index ARR	0.5	0.3	0.4	0.5	0.0	0.0	0.0
ARR Reduction	0.7	1.0	1.0	0.5	0.7	1.8	2.5
ARR Reduction %	58.8	77.4	71.9	50.0	100.0	100.0	100.0

Table 3: Average WHOQOL-BREF raw domain scores with (standard deviation)

Drug groups→ Domains ↓	DMF	TFM	IFNβ 1a	Peg-IFNβ 1a	GA	RTX	NTZ
1. Physical Health (Max-35)	21.3 (3.4)	22.7 (4.7)	19.5 (4.2)	17.8 (2.9)	21.7 (4.0)	21.0 (5.2)	14.5 (10.6)
2. Psychological (Max-30)	19.3 (4.6)	21.3 (4.0)	15.7 (4.3)	17.0 (5.1)	18.0 (6.1)	15.8 (4.4)	15.0 (12.7)
3. Social Relationships (Max-15)	9.7 (2.4)	10.6 (2.0)	9.2 (2.4)	10.8 (2.5)	10.0 (2.7)	9.3 (2.9)	12.0 (2.8)
4. Environment (Max-40)	28.6 (3.6)	27.8 (5.2)	26.0 (5.7)	29.0 (8.2)	29.0 (5.3)	25.3 (4.1)	29.0 (11.3)

Socio-economic status

MKSS was used to assess the affordability of the DMT as per the socioeconomic strata. The average MKSS score of each DMT group was calculated. DMF, IFNβ 1a, peg-IFNβ 1a, rituximab, and GA are affordable to the upper middle class and above and teriflunomide to the lower middle class and above. Data shows natalizumab was the most expensive and could be afforded only by high-class strata patients. This information has been graphically represented in Figure 1.

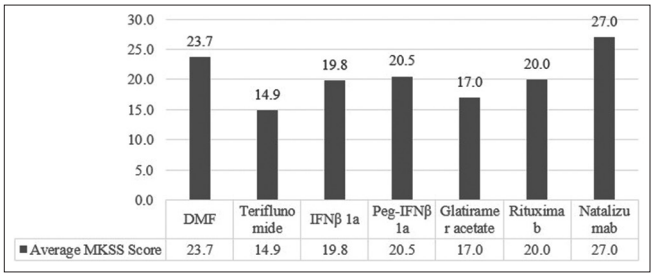

Figure 1: Socioeconomic class associated affordability of each DMT group

Cost of DMT

The total cost of DMT for MS treatment is unknown in India. The cost depends on the drug used, biosimilar/manufacturer/distributor, dosage, price per unit in Indian rupee and frequency, dosage form, duration of administration, severity, and type of the disease. This information about the DMT, that is, agent name, active pharmaceutical ingredient, and mode of administration was captured in this study for easy comparison. Natalizumab had the highest annual cost, while teriflunomide was the most affordable [Table 4].

Cost-effectiveness analysis

Subjective data was collected to assess the impact of DMT-related expenses on participants and their families. Savings exhaustion was higher in injectable/infusion DMT groups (>40%) than in oral DMT groups (<40%). Compromise on necessities due to the affordability of DMT was low in most DMT groups except in Peg-IFNβ 1a group (50%). Dependence on the family was significant in every group (>60%). DMT costs impacted family well-being and recreational activities to varying degrees in each group [Table 5].

Rating of disease (ROD)

A subjective numerical expression of the relative likeability of DMTs was carried out. Participants were asked to rate their satisfaction with the DMTs they were using on a scale of 1 to 10 based on availability, affordability, effectiveness, ease of administration, and impact on QoL. The average of these ratings from each group has been presented here in the form of ROD for both branded and biosimilars. Rituximab had the highest average rating of 9.0, while Peg-IFNβ 1a had the lowest average rating of 3.5. The ROD of biosimilars in every DMT group was either better or equal to brand-name DMTs [Figure 2].

Adverse drug reactions

Of the 69 study participants, 12 (17.4%) reported major side effects requiring medical attention, including anaphylaxis, breathlessness, liver toxicity, and lymphocytopenia, but no deaths occurred. Common side effects varied among the DMT groups. In the DMF group, hair fall and flushing were common, while liver toxicity and lymphocytopenia were reported in only one patient. Teriflunomide caused hair fall in the majority (58%) of participants. IFNβ 1a caused fever (100%) and chills (53%) and generalized body weakness (53%), mood swings (35%), and depression (24%) were also reported, while Peg-IFNβ 1a caused these as well as nausea and vomiting in 100% patients. GA caused injection site reactions in 50% of cases and anaphylaxis in 25% (1 participant). Rituximab caused breathlessness during infusion in 60% and anaphylaxis and anemia in 20% (1 participant) of cases. Natalizumab was very well tolerated.

Discussion

In the Indian MS scenario, this study provides an extensive database of efficacy, cost-effectiveness, and affordability of most of the MS DMTs available in the Indian market. Newly diagnosed MS patients often are not fortunate enough to have adequate time with the treating neurologist to clear all their queries, considering the average consultation time in India which stands at 1.9 minutes.[12] Treatment of MS is certainly much more complex as the outcomes of treatment are highly influenced by the disease severity of the patient.[13] Indians have poor insurance coverage, with little aid from the government for this particular disease.[4] Most private insurance companies do not cover MS, and those who cover, ask for a cooling period of 5 years. Unlike the Western countries, the total cost of treatment is unknown, added to the

Table 4: Annual cost of study DMTs with dosage, price per unit in Indian Rupees, and frequency of administration

ROA	DMT Agent	Active Pharmaceutical Ingredient	Biosimilar /Manufacturer/ Distributor	Dosage	Cost per Unit (₹)*	Frequency†	Annual cost of DMT
Oral DMTs	Fingomod	Fingolimod	Sun Pharmaceuticals	0.5 mg	₹89	Daily	₹32485
	Aubagio§	Teriflunomide	Genzyme (Sanofi)	7 mg	~₹1200-1300‡	Daily	₹438000-474500
	Scleteri	Teriflunomide	Sun Pharmaceuticals	7 mg	₹60	Daily	₹21900
	Teru MS	Teriflunomide	MSN Laboratories	7 mg	₹69	Daily	₹25156
	Denopsy	Teriflunomide	Natco Pharmaceuticals	14 mg	₹114	Daily	₹41610
	Merosya	Teriflunomide	Intas Pharmaceuticals	7 mg	₹60	Daily	₹21900
	Tecfidera§	Dimethyl fumarate	Eisai Pharmaceuticals	120 mg	₹1607	Daily	₹586555
	Sclerogem	Dimethyl fumarate	Cipla Pharmaceuticals	120 mg	₹116	Daily	₹42340
	Sclerifuma	Dimethyl fumarate	Sun Pharmaceuticals	120 mg	₹33	Daily	₹11972
	MS 120	Dimethyl fumarate	MSN Laboratories	120 mg	₹28	Daily	₹10220
	Dyfira	Dimethyl fumarate	Intas Pharmaceuticals	120 mg	₹55	Daily	₹20153
Injectable DMTs	Avonex§	Interferon Beta 1a	Biogen Inc.	30 mcg	₹9557	Once weekly	₹496964
	Relibeta	Interferon Beta 1a	Reliance Life Sciences	30 mcg	₹6785	Once weekly	₹352820
	Rebif§	Interferon Beta 1a	Merck & Co.	44 mcg	₹6030	Once weekly	₹313560
	Plegridy§	Pegylated Interferon Beta 1a	Biogen Inc.	125 mcg	~₹16000-₹30000‡	Once every 14 days	₹416000-780000
	Glatimer	Glatiramer acetate	Natco Pharmaceuticals	20 mg	₹990	Daily	₹361350
	Glatirex	Glatiramer acetate	Intas Pharmaceuticals	20 mg	₹970	Daily	₹354050
Infusion DMTs	Tysabri§	Natalizumab	Eisai Pharmaceuticals	300 mg	₹108702	Once every 28 days	₹1304424
	Ristova	Rituximab	Roche Pharma	500 mg	₹38047	Once every 6-12 months	₹38047-76094
	Toritz T	Rituximab	Torrent Pharmaceuticals	500 mg	₹36946	Once every 6-12 months	₹36946-73892
	Reditux	Rituximab	Dr.Reddy's laboratories	500 mg	₹38047	Once every 6-12 months	₹38047-76094
	Ikgdar	Rituximab	Cipla Pharmaceuticals	500 mg	₹38047	Once every 6-12 months	₹38047-76094
	Lupiximab	Rituximab	Lupin Limited	500 mg	₹23125	Once every 6-12 months	₹23125-46250
	Rituxipan	Rituximab	Mankind Pharma Ltd	500 mg	₹38047	Once every 6-12 months	₹38047-76094

*All prices are based on information obtained from TATA 1mg website (www. 1mg.com) (May 2023) and are subject to change, †Frequency of dosage may vary in different phases of treatment, ‡These prices are based on information obtained from the participants, §Brand name of DMTs

Table 5: Cost-effectiveness analysis using subjective data

Drug Group→ Cost Effect ↓	DMF	TFM	IFNβ 1a	Peg-IFNβ 1a	GA	RTX	NTZ
Savings Exhaustion	9 (34.6%)	3 (25.0%)	10 (58.8%)	2 (50.0%)	2 (66.7%)	2 (40.0%)	1 (50.0%)
Compromise on basic necessity	2 (7.7%)	2 (16.7%)	2 (11.8%)	2 (50.0%)	1 (33.3%)	0.0	0.0
Dependence on family	16 (61.5%)	11 (91.7%)	12 (70.6%)	4 (100.0%)	3 (100.0%)	4 (80.0%)	2 (100.0%)
Mental health disturbed	8 (30.8%)	3 (25.0%)	8 (47.1%)	3 (75.0%)	2 (66.7%)	2 (40.0%)	0.0
Cost associated depression	5 (19.2%)	3 (25.0%)	5 (29.4%)	2 (50.0%)	2 (66.7%)	1 (20.0%)	0.0
Family well-being affected due to cost	6 (23.1%)	5 (41.7%)	8 (47.1%)	3 (75.0%)	2 (66.7%)	2 (40.0%)	1 (50.0%)
Recreational and leisure activities affected	12 (46.2%)	5 (41.7%)	16 (94.1%)	4 (100.0%)	2 (66.7%)	2 (40.0%)	1 (50.0%)

drug cost is the repeated cost of hospitalization, consultation fee, MRI fee, regular follow-up, and disability-related services. These issues have considerable implications on the QoL of MSPs and their families, friends, and the cost to society. Unlike the Boster *et al*. efficacy study,[14] in our study, ARR was coupled with the impact of the DMT on the QoL of the participants to develop a better picture of the real-world efficacy of the DMTs. This study shows oral teriflunomide stands out as a DMT which has acceptable efficacy while maintaining good affordability and QoL probably because of the availability of effective and affordable biosimilars.

The greatest negative impact on QoL was reported to be that of the injectable DMTs, that is, IFNβ 1a and Peg-IFNβ 1a, probably because of the mentioned adverse effects and high annual cost which culminates in poor rating of DMT. The efficacy of infusion DMTs, that is, natalizumab and rituximab reported in this study was similar to a systemic review and meta-analysis study conducted in 2019 in the United States of America which concluded that monoclonal antibodies not only decreased the relapse rate but also prevented disability progression.[15] WHOQOL-BREF scores had a strong negative correlation with the severity of

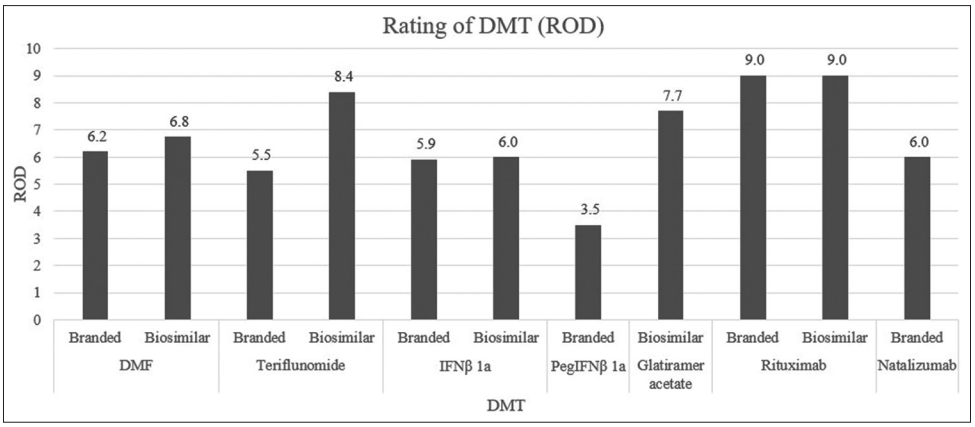

Figure 2: Rating of DMT

disease and annual cost of the DMT indicating that both these factors contributed to lowering the QoL of the participant. The Indian pharmaceutical industry is the 3rd largest[4] in the world and has developed a tremendous capacity for manufacturing biologicals. In a country like India where the per capita GDP stands at the level of less than ₹16000 per month,[16] biosimilar medications are highly beneficial for the low-income group of MS patients. This study's ROD analysis substantiates this claim, showing that the ROD of biosimilars was either superior or at least equivalent to that of the branded DMTs. The database of annual cost of DMT created through this study along with the socioeconomic class associated affordability will guide the treating neurologist in selecting the right DMTs appropriately suited to the patient's finances. In the study by Aruru MV and Salmon WJ, the cost of the DMTs mentioned was a conversion of United States Dollar (USD) prices to Indian Rupee (INR).[4] This doesn't give us an exact idea of Indian market prices or the affordability of the medications in the real world. As it was observed in this study, the cost of these medications for the end user, that is, MS patient, varied greatly across India depending on geographical location and pharmacy, hence cost alone certainly wasn't the right basis for comparison of affordability of the DMTs. The Modified Kuppuswamy socioeconomic scale scores set forth the reality that the lower socioeconomic class doesn't have many options in terms of MS DMTs. Savings exhaustion and dependence on the family for affording the DMT were reported from every DMT group reiterating the impact of the cost of the DMT on the patients and their families. Rituximab, possibly because of its insurance coverage, wider availability of affordable biosimilars, less frequency of administration, and high efficacy had the highest ROD.

Study limitations

The costs associated with periodic MRI scans, doctor consultation fees, DMT administration, hospitalization, and micronutrient supplements that can further increase the cost of MS treatment were not assessed in this study. In the prevailing COVID-19 situation, researchers couldn't assess participants' degree of disability using EDSS (Expanded disability status scale) due to the virtual nature of study interviews. Patients with confounding factors and morbidities, which can affect the study parameters (efficacy of DMTs, socioeconomic class, and QoL), were not considered for this study. The study's retrospective nature can result in recall bias while reporting bias may occur due to the social stigma attached to neurological diseases in India. Future iterations of the study can address these limitations.

Conclusion

MS, from diagnosis up to and beyond the treatment (which may last lifelong), is an expensive disease. This study highlights significant differences in efficacy and QoL impact among all MS DMT groups in India. The study created a database of each DMT group's annual cost and socioeconomic class-associated affordability based on the Indian market. The real-world information on efficacy and cost-effectiveness will aid doctors and patients in making treatment decisions and estimating financial and QoL impacts associated with each DMT.

Financial support and sponsorship

The study was financed by ICMR under the short-term studentship (STS) program for the year 2020-21. Multiple Sclerosis Society of India (MSSI) facilitated the enrolment of participants in the study.

Conflicts of interest

There are no conflicts of interest.

References

1. Pandit L, Murthy JM. Treatment of multiple sclerosis. Ann Indian Acad Neurol 2011;14(Suppl 1): S65-9. doi: 10.4103/0972-2327.83094.
2. Hartung DM. Health economics of disease-modifying therapy for multiple sclerosis in the United States. Ther Adv Neurol Disord 2021;14:1756286420987031. doi: 10.1177/1756286420987031.
3. Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, *et al*. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler 2020;26:1816-21.
4. Aruru MV, Salmon WJ. Multiple sclerosis in India: Drivers of access and affordability. MOJ Public Health 2019;8:1-6. doi: 10.15406/mojph.2019.08.00275.
5. Biswkarma VK, Wadhawan S. Emerging role of pharmacoeconomics

into clinical trials and its outcomes: An overview. Indian J Pharm Pharmacol 2014;7:66-72.
6. Bhatia M, Singh DP. Health sector allocation in India's budget (2021–2022): A trick or treat? Int J Community Soc Dev 2021;3:177-80.
7. 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;17:162-73.
8. Indian council of medical research 2017. National ethical guidelines for biomedical and health research involving human participants. Section-2.3 Privacy and Confidentiality- General Ethical Issues [Internet] [cited June 6 2021]. Available from: https://main.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf.
9. Lavery AM, Verhey LH, Waldman AT. Outcome measures in relapsing-remitting multiple sclerosis: Capturing disability and disease progression in clinical trials. Mult Scler Int 2014;2014:262350. doi: 10.1155/2014/262350.
10. Skevington SM, Lotfy M, O'Connell KA, WHOQOL Group. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial. A report from the WHOQOL group. Qual Life Res 2004;13:299-310.
11. Saleem SM, Jan SS. Modified Kuppuswamy socioeconomic scale updated for the year 2021. Indian J Forensic Community Med 2021;8:1-3. doi: 10.18231/j.ijfcm. 2021.001
12. Irving G, Neves AL, Dambha-Miller H, Oishi A, Tagashira H, Verho A, *et al*. International variations in primary care physician consultation time: A systematic review of 67 countries. BMJ Open 2017;7:e017902. doi: 10.1136/bmjopen-2017-017902.
13. Hersh CM, Hua LH. Comparative effectiveness studies in multiple sclerosis. Neurodegener Dis Manag 2020;10:113-8.
14. Boster A, Nicholas J, Wu N, Yeh WS, Fay M, Edwards M, *et al*. Comparative effectiveness research of disease-modifying therapies for the management of multiple sclerosis: Analysis of a large health insurance claims database. Neurol Ther 2017;6:91-102.
15. Li H, Hu F, Zhang Y, Li K. Comparative efficacy and acceptability of disease-modifying therapies in patients with relapsing-remitting multiple sclerosis: A systematic review and network meta-analysis. J Neurol 2020;267:3489-98.
16. World Development Indicators | DataBank [Internet]. Worldbank.org. [cited May 2 2023]. Available from: https://databank.worldbank.org/reports.aspx?source=2&series=NY.GDP.PCAP.CD&country=IND#advancedDownloadOptions.