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OCRELIZUMAB IN MULTIPLE SCLEROSIS: REAL-WORLD EXPERIENCE FROM BALOCHISTAN, PAKISTAN

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ABSTRACT

Background and objective:

Multiple sclerosis (MS) is an autoimmune demyelinating disorder affecting the central nervous system. Ocrelizumab, a disease-modifying drug for MS, is funded by Bait ul Maal Pakistan for economically disadvantaged patients in Balochistan. The objective of this study was to evaluate the treatment response of Ocrelizumab in our population.

Methods:

This prospective observational study enrolled 22 patients from three tertiary care hospitals in Balochistan from July 2021 to June 2022. Patients aged 18–50 years diagnosed with MS and without contraindications for Ocrelizumab were included. The Expanded Disability Status Scale (EDSS) was calculated at baseline and at three, six, and 12 months. Patient satisfaction was assessed using a Likert scale (1 = extremely unsatisfied, 5 = extremely satisfied). Primary outcome was EDSS improvement; secondary outcomes included patient and family satisfaction.

Results:

Of 22 patients, 14 were female and 8 were male, with a mean age of 33.23 ± 9.75 years. RRMS was most common (81%; n=18), followed by primary progressive MS (14%; n=3). Median EDSS improved from 5.36 ± 2.50 at baseline to 3.37 ± 2.98 at follow-up. Major improvement was seen in 20% of patients, mild improvement in 50%, and no change/worsening in 30%. Patient and family satisfaction scores were 3.14 ± 1.42 and 3.10 ± 1.30, respectively.

Conclusion:

Ocrelizumab is an effective, safe, and acceptable treatment for MS patients in our population. EDSS scores improved significantly from 5.36 to 3.37 at the end of the follow-up period. Both patient and family satisfaction rates were high, indicating positive real-life experiences with the treatment.

Keywords: Multiple Sclerosis, Disease modifying drugs (DMD), Expanded disability status scale (EDSS), Ocrelizumab

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune inflammatory disorder of central nervous system (CNS), involving both the brain and the spinal cord. It is characterized by demyelination, axonal degeneration, and ultimately neurodegeneration and loss of CNS tissue.[1,2] Global burden of MS until 2016 was estimated at 2.22%, being the 10th leading cause of disease burden.[3] Estimated prevalence in the Pakistani population is 10 per 100,000.[4] MS usually affects individuals aged 20–40 years and is associated with progressive disability over time. The predominant MS variant is relapsing-remitting MS (RRMS), affecting 85% of patients, while 10-15% of cases present with a primary progressive variant (PPMS).[5,6] The MS treatment with disease-modifying therapies (DMTs) is prohibitively expensive, and limiting access for many patients. Fortunately, Ocrelizumab, one of the DMTs, is funded by Bait-ul-Maal Pakistan (a government-funded charitable organization) for economically disadvantaged patients.

Ocrelizumab is an FDA-approved treatment for both RRMS and PPMS. It has been shown to reduce disability progression by 6.2% and brain atrophy by 17.5%.[7] Considering the younger population affected

by this disease, Ocrelizumab's effectiveness in younger populations with high disease activity makes it a favorable choice.[8,9] Despite its potential, there is a lack of studies evaluating its efficacy, disability improvement, adherence, and real-world experiences in Pakistan. Our study aims to address this gap by providing locally relevant evidence on Ocrelizumab's effectiveness, safety, patient satisfaction, and acceptability among MS patients.

METHODS

This was a prospective study using universal sampling and was conducted across three tertiary care hospitals in Balochistan province between July 2021 to June 2022. It was approved by the Institutional Review Board of Bolan University of Medical and Health Sciences, Quetta (No.16/BUMHS/IRB). All adult patients, aged 18 to 50 years, diagnosed with MS by a certified neurologist and receiving Ocrelizumab were referred to the authors of this study. Patients from varied socioeconomic backgrounds were included, including those who self-funded Ocrelizumab or received it through financial assistance programs such as Bait-ul-Mal.

The MS diagnosis was made according to the revised 2017 McDonald Criteria. For the first treatment, Ocrelizumab was given in two divided doses, two weeks apart (at week 0 and week 2), and then subsequent infusions were administered every six months (600 mg IV). All patients underwent scheduled examinations, and their records were reviewed before treatment and at three, six, and 12 months after receiving Ocrelizumab.

Exclusion criteria included unconfirmed MS cases, patients not evaluated by a neurologist, significant coexisting medical conditions (such as uncontrolled diabetes mellitus, ischemic heart disease, and chronic infections like tuberculosis, hepatitis B, and C), and a history of COVID infection or vaccination within 6 weeks.

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were reported as mean ± standard deviation (SD) and range, while categorical variables were presented as frequencies and percentages. A paired t-test was used to compare pre- and post-treatment EDSS scores. Bivariate analysis was performed to assess associations between Ocrelizumab efficacy and patient characteristics. A p-value < 0.05 was considered statistically significant.

RESULTS

We enrolled 22 patients: 14 females (63.6%) and 8 males (36.4%), with a mean age of 33.23 ± 9.75 years (range: 18-48). Unfortunately, two patients were lost to follow-up. The mean Ocrelizumab doses received were 2.64 ± 1.002 (range: 1-4). Their average disease duration was 2.9 ± 2.42 year (range: 0.5-8.5 (Table).

Table 1: Basic Demographics and disease related details of MS patients (n = 22)		
Age	Mean ± SD (years)	33.23 ± 9.75
Gender	Male Female	8 (36.4%) 14 (63.6%)
Marital status	Married Unmarried	14 (63.6%) 8 (36.4%)
Affordability for Ocrelizumab	Can afford Cannot afford	1 (4.5%) 21 (95.5%)
Duration of Symptoms	< 1 year 1-2 years > 2 years	4 (18.2%) 9 (40.9%) 9 (40.9%)
Multiple Sclerosis Type	Relapsing Remitting MS Primary Progressive MS Clinically Isolated Syndrome	18 (81.8%) 3 (13.6%) 1 (4.5%)
MRI Findings	MS findings detected Non-specific	19 (86.4%) 3 (13.6%)
VEP	Consistent with Optic Neuritis Normal Not done	7 (31.8%) 2 (9.1) 13 (59%)
EDSS	EDSS Pre-Ocrelizumab EDSS Post-Ocrelizumab Difference of EDSS score pre and post Ocrelizumab therapy	5.364 ^ 3.375 ^ 1.875 ^
Satisfaction with Ocrelizumab treatment (score: 1-5)	Patient satisfaction Family satisfaction	3.14 ^ 3.10 ^
^ mean EDSS = Expanded Disability Status Scale; MRI = Magnetic resonance		

Among the types of MS, RRMS was the most common (81%, n=18), followed by PPMS (13.6%, n=3). Figure 1 shows the predominant presenting MS symptoms, while Figure 2 shows symptom improvement following Ocrelizumab therapy. Thirty-six percent of patients had improvement in all symptoms, while 13.6% had no improvement in any symptoms with the use of Ocrelizumab.

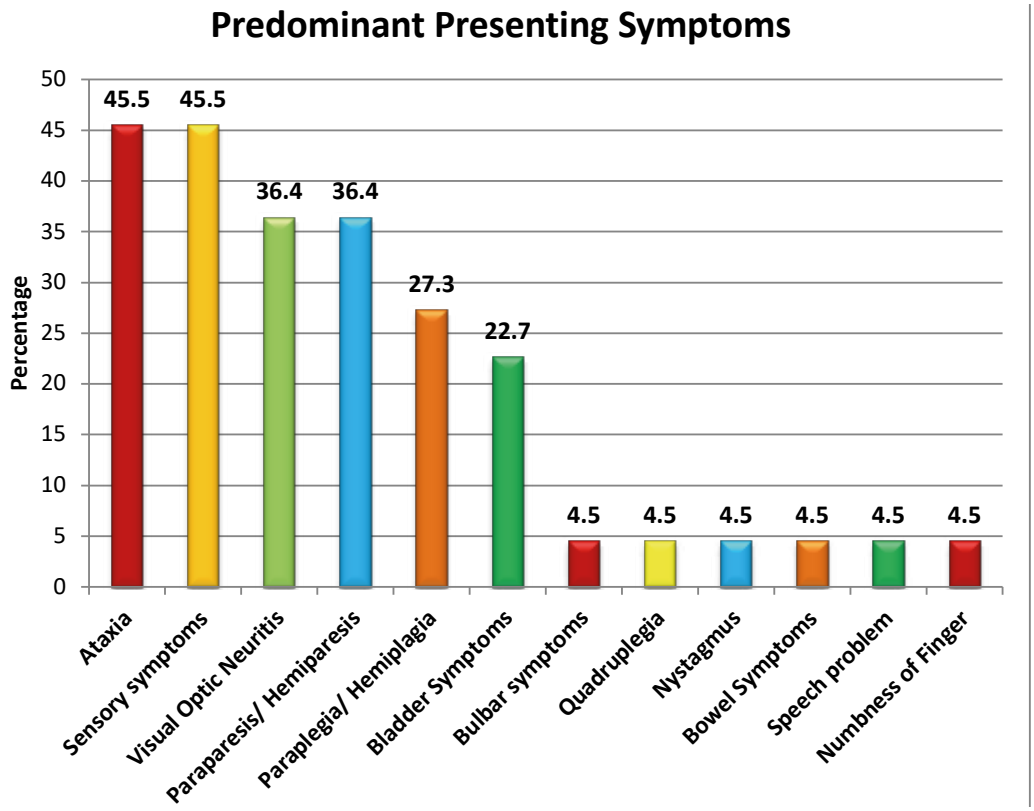

Figure 1: Predominant symptoms with which patients presented initially

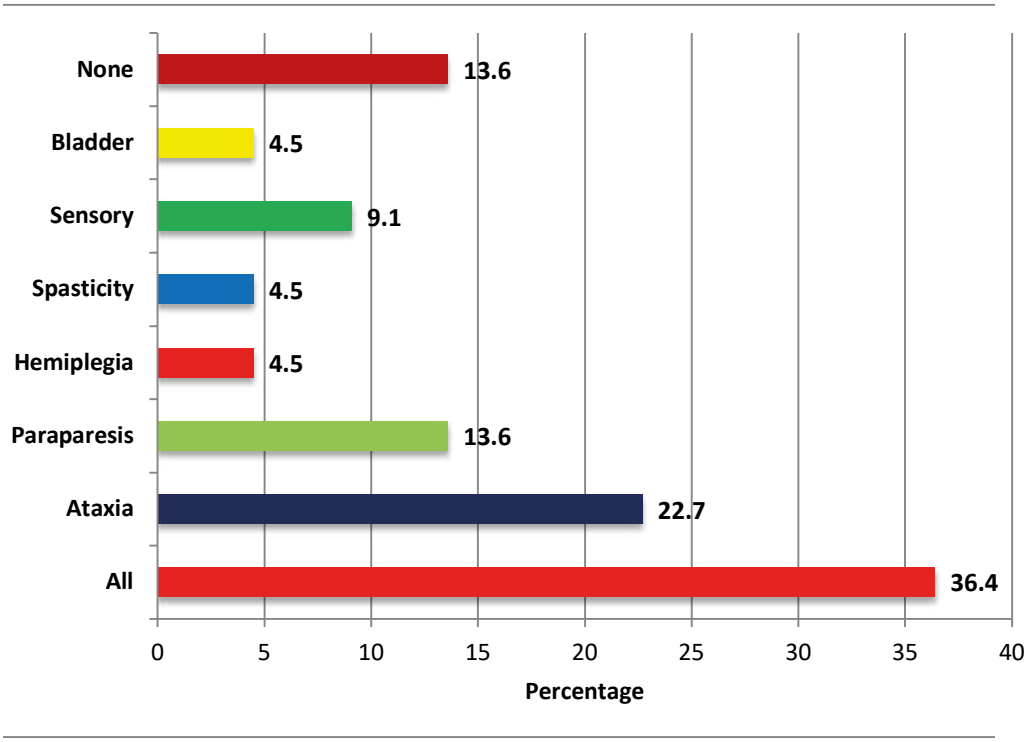

Figure 2: Symptoms improvement after Ocrelizumab therapy

The mean EDSS before Ocrelizumab was 5.36 ± 2.50, which reduced to 3.37 ± 2.98 on follow- up visits. The difference was statistically significant when tested through a paired t-test ($p < 0.0001$, Table 1). Nearly half of all patients and their family members were satisfied, while a quarter of all patients and their family members were not satisfied with the results of Ocrelizumab (Figure 3).

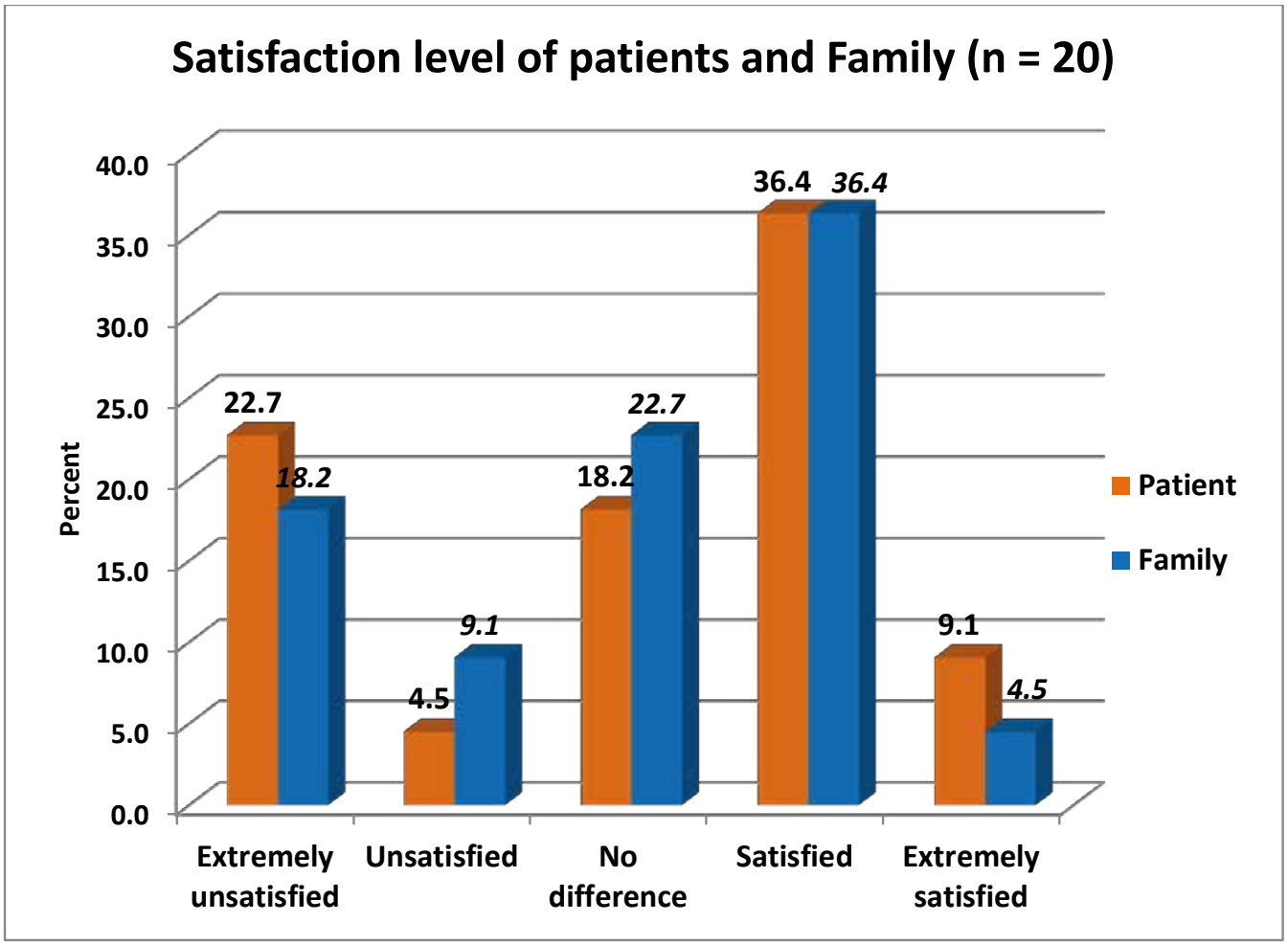

Figure 3: Comparison of level of satisfaction of patients and family with Ocrelizumab therapy

There was more efficacy of Ocrelizumab noted in female patients compared to males; however, the difference was not statistically significant ($p = 0.846$). Likewise, patients who presented with RRMS had higher efficacy of Ocrelizumab compared to PPMS ($p = 0.016$).

DISCUSSION

The high cost of multiple sclerosis (MS) treatment poses a significant challenge, particularly in developing countries like ours. Fortunately, in Balochistan, Ocrelizumab is being provided to underserved patients through a public sector welfare organization. Ocrelizumab is a humanized monoclonal anti-CD20 antibody approved for treating the relapsing and primary progressive forms of MS (RMS and PPMS, respectively) based on findings of large trials.[8,9] Ocrelizumab effectively prevents clinical and subclinical disease activity and disease progression compared to interferon-beta treatment. We conducted a prospective study to evaluate efficacy, disability improvement, and patient satisfaction in our population. To the best of our

knowledge, this is the first study of its kind in our region.

At the one-year follow-up, 20% of patients demonstrated excellent clinical outcomes, while 18% were completely free of MS symptoms. Significant symptomatic improvement was observed in 50% of our patients, whereas 30% experienced no change or disease progression. Notably, there was significant improvement in ataxia, paraparesis/hemiparesis, and sensory symptoms. A study by Rojas J and coworkers reported a higher rate of MS relapse (62%; p value = 0.01) with Ocrelizumab. 10 The OPERA I (WA21092; n=821) and OPERA II (WA21093; n=835) were also shown to have lower rates of clinical and MRI progression compared to placebo in the double-blind, parallel-group trials.[11,12] Following Ocrelizumab infusion, 37% of participants experienced new symptoms, including fatigue, flu-like symptoms, and walking difficulties, which resolved within two weeks.[13]

In our current study, 10% of patients experienced depression, movement restriction, or bladder issues as side effects of Ocrelizumab, while 25% reported no side effects. Toorop AA, et al. reported the most frequent side effects were fatigue, cognitive disability, and sensory symptoms.[14] Other studies documented only mild to moderate side effects.[13,15,16] Thus, Ocrelizumab is both effective and safe. Studies have shown that after one year of treatment with Ocrelizumab, patients experienced improved health-related quality of life, relief from clinical symptoms, and reduced dependence on DMTs.[15-17] Contrary to this a few studies reported relapse in fewer than 20% of patients at follow-up.[18] Sempere AP, et al.;[19] found that in PPMS patients, the rates of disease progression were generally higher; while other studies detected no significant changes were reported in either patient of RRMS & PPMS.[12,20-22]

A significant reduction in the mean EDSS score was observed, decreasing from 5.25 ± 2.5 to 3.37 ± 2.98 ($p < 0.001$). Based on this, disability improvement—defined as a decrease in EDSS score for ≥3 months (by 0.5 points if baseline EDSS >6.5 or 1 point if baseline EDSS <6.0)—was achieved in 75% of cases (n = 15) The study by Pereira-Coutinho, et al., comparing their retrospective cohort patients small sample (n = 16) as a "control group" to other clinical trial cohorts found significant differences in EDSS progression and MRI activity.[23] Boziki, M., et al., in their study found that mean ± SD EDSS difference of 4.91 ± 0.3.[24] Montalban X, et al., found that mean EDSS difference from 2 to 6.5 at baseline with the use of Ocrelizumab,[20] while Toorop AA, et al., reported a difference in EDSS of 3 maximum (5.5-2.5) with a mean of 3.8.[14] Contrary to this a study by Coban H, found no change in EDSS scores in different ethnicities exposed to ocrelizumab.[25]

Mean ± SD age noted in our study was 33.23 ± 9.75 years (18-48) which resembles to other contemporary studies like 48.5 ± 1.69 years,[24] 44.7 +7.9 years 7, 42.8 ± 11 years.[14] The proportion of female gender was 63.6% in our study while others noted 45%-62% of females in their study.[16,20,26] Regarding age and gender, higher Ocrelizumab efficacy was observed in female patients and those in their third decade of life ($p = 0.846$ and $p = 0.353$, respectively).

Younger age, shorter disease duration, and RRMS have been identified as favorable factors for Ocrelizumab efficacy. In our bivariate analysis, higher efficacy was observed in patients with a shorter disease duration ($p = 0.134$) and those with RRMS ($p = 0.016$) compared to PPMS. Body mass index also has its effect, as found by Toorop AA et al.,[16] that higher BMI (BMI ≥25) is associated with higher rates of wearing-off phenomenon of Ocrelizumab. The proportion of MRI efficacy, defined as the absence of new/enlarged T2 lesions on the brain and cervical MRI, was >90% at 12- and 24-months, but we did not evaluate this.

Infusion-related reactions (IRRs) are common, especially after the first infusion, occurring in 34.3% of RRMS and 40.1% of PPMS cases. To minimize IRRs and enhance tolerability, Ocrelizumab infusion should be preceded by corticosteroids and antihistamines under specialist supervision.[26] In our study, two patients were lost to follow-up, and two discontinued treatment due to lack of efficacy. No significant adverse events or tolerability issues were reported. Patient and family satisfaction was high, with mean satisfaction scores of 3.14 ± 1.42 for patients and 3.10 ± 1.30 for families ($p = 0.029$ & 0.011, respectively). While Ocrelizumab demonstrated satisfactory clinical outcomes, comparative studies remain limited in size and may be subject to bias, particularly due to residual confounding.

Our study has certain limitations. Firstly, there was no control group to compare the effectiveness; Secondly, its observational design might have been exposed to bias. We recruited as many participants as possible

from our tertiary care setups; however, the small sample size may have led to statistical limitations. Nevertheless, our current study provides real-time evidence from a developing country that will help and guide the care-providers to manage the MS patients better.

CONCLUSION

Ocrelizumab proved to be an effective, safe, and well-tolerated treatment in our population, with EDSS improving from 5.36 to 3.37 by the end of the follow-up period. Both patient and family satisfaction rates were high, and side effects were minimal.

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Ahmed Wali; design, data collection, data analysis, manuscript writing
Sajid Hameed; concept, data analysis, manuscript writing
Hazar Khan; data collection, manuscript writing
Amara Ahmed; data collection, manuscript revision
Madiha Malik; concept, design, manuscript writing

All the authors have approved the final version to be published, and agree to be accountable for all aspects of the work.