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MYASTHENIA GRAVIS IN INDIA:A BREIF CASE STUDY

KEY WORDS: Myasthenia gravis, India, autoimmune disorders, healthcare disparities, neuromuscular diseases

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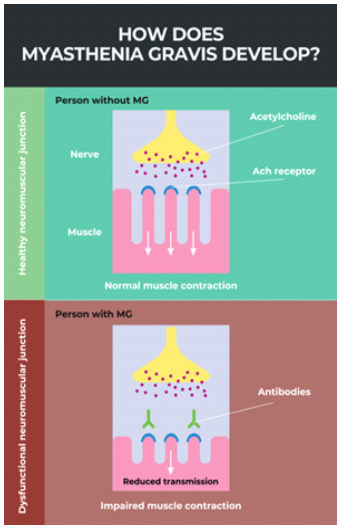
ABSTRACT

Myasthenia gravis (MG), a rare autoimmune neuromuscular disorder, poses significant diagnostic and therapeutic challenges in India. Characterized by muscle weakness and fatigue, MG disproportionately impacts quality of life in low-resource settings. This article explores the epidemiology of MG in Rural and Urban India, regional disparities in healthcare access, sociocultural barriers, and advancements in treatment. It underscores the need for increased awareness, multidisciplinary care, and policy reforms to address gaps in managing this chronic condition.

INTRODUCTION

Myasthenia gravis (MG), a prototypical autoimmune neuromuscular junction disorder, is characterized by pathogenic autoantibodies targeting postsynaptic acetylcholine receptors (AChRs), muscle-specific kinase (MuSK), or lipoprotein-related protein 4 (LRP4), culminating in impaired neuromuscular transmission and fluctuating skeletal muscle weakness (Gilhus et al., 2019). The immunopathogenesis involves complement-mediated destruction of the postsynaptic membrane, antibody-dependent internalization of AChRs, and thymic abnormalities such as follicular hyperplasia or thymoma, which perpetuate autoreactive B-cell activity (Deymeer et al., 2021). Globally, epidemiological studies report a heterogenous prevalence of 15–179 cases per million, with age-specific peaks in women aged 20–40 years and men over 60 years (Dalakas, 2020). In India, however, MG remains underrecognized due to diagnostic lacunae, with seroprevalence studies limited to urban tertiary centers and a paucity of population-based data (Das & Khadilkar, 2022). Compounding this issue are multifaceted challenges, including delayed clinical suspicion among primary care physicians, restricted access to serological assays (e.g., AChR/MuSK antibody testing via radioimmunoprecipitation), and socioeconomic impediments such as out-of-pocket expenditures for advanced diagnostics like single-fiber electromyography (SFEMG) (Nair et al., 2019).



Neuromuscular junction in Myasthenia Gravis(Shapiro, 2025)

The Indian healthcare ecosystem, marked by urban-rural dichotomies in infrastructure, exacerbates disparities. Rural populations, constituting 65% of India's 1.4 billion inhabitants, frequently encounter barriers such as geographic inaccessibility to neuroimmunology specialists, inadequate stocks of acetylcholinesterase inhibitors (e.g., pyridostigmine bromide), and limited critical care resources for managing myasthenic crises, including ventilator support and rapid immunomodulatory therapies like intravenous immunoglobulin (IVIG) or plasmapheresis (Chaudhuri et al., 2022). Furthermore, cultural narratives often conflate early MG symptoms—ptosis, dysphagia, or proximal limb weakness—with non-medical etiologies, fostering reliance on alternative medicine and delaying evidence-based interventions (Tripathi et al., 2020). Despite these hurdles, emerging initiatives such as tele-neurology platforms and multidisciplinary MG clinics in metropolitan hubs aim to bridge gaps in care delivery (Joshi, 2023). Concurrently, research into cost-effective immunosuppressive regimens (e.g., tacrolimus, mycophenolate mofetil) and advocacy for inclusion of MG therapies in national health insurance schemes (e.g., Ayushman Bharat) signal incremental progress toward equitable management (ICMR, 2022).

Prevalence and Demographics

Studies suggest MG prevalence in India is comparable to global estimates, with a reported incidence of 10–20 cases per million annually (Das & Khadilkar, 2022). However, regional variations exist. For instance, tertiary care centers in Maharashtra and Karnataka report higher case loads, likely due to better diagnostic facilities (Nagaraja et al., 2020). Pediatric-onset MG accounts for 10–15% of cases in India, slightly higher than Western cohorts (Singhal et al., 2021).

Genetic and Environmental Factors

Genetic predisposition plays a role, with HLA-B8 and DR3 alleles linked to MG susceptibility in Indian populations (Pandey & Mishra, 2019). Environmental triggers, such as infections (e.g., malaria, tuberculosis) and vitamin D deficiency, are prevalent in India and may exacerbate autoimmune responses (Gupta et al., 2020).

Clinical Presentation and Diagnosis

Indian patients with myasthenia gravis (MG) frequently manifest initial symptomatology in the extraocular musculature, presenting as levator palpebrae weakness (ptosis) and binocular diplopia due to impaired

neuromuscular transmission in the oculomotor, trochlear, or abducens nerves (Joshi et al., 2021). This ophthalmoparetic phase often progresses to generalized myasthenia within 12–18 months, characterized by fatigable weakness in axial and appendicular muscle groups, including proximal limb girdle muscles (e.g., deltoids, iliopsoas) and respiratory muscles, potentially culminating in myasthenic crisis—a life-threatening exacerbation marked by acute respiratory insufficiency (Vincent et al., 2020).

Approximately 30–40% of patients develop bulbar palsy, involving dysfunction of the oropharyngeal musculature, which manifests as dysphagia (impaired deglutition), dysarthria (slurred speech due to palatal weakness), and masticatory fatigue (Sharma et al., 2020). Bulbar involvement correlates with heightened morbidity due to risks of aspiration pneumonia and nutritional deficits, while delayed initiation of immunomodulatory therapies (e.g., corticosteroids, rituximab) exacerbates mortality, particularly in resource-limited settings lacking access to non-invasive ventilation (NIV) or plasmapheresis (PLEX) (Goyal et al., 2022).

Diagnostic Challenges

Diagnosis relies on clinical evaluation, antibody testing (AChR, MuSK), and electrodiagnostic studies. However, in India:

1. Limited Access to Antibody Testing: Only 30% of rural clinics have facilities for AChR antibody assays (Nair et al., 2019).
2. Electrodiagnostic Barriers: Repetitive nerve stimulation (RNS) and single-fiber electromyography (SFEMG) are available in <15% of neurology departments (Rao et al., 2022).
3. Delayed Diagnosis: Median time to diagnosis is 2–3 years, leading to preventable complications (Kumar et al., 2021).

TREATMENT

Pharmacological Management

The therapeutic armamentarium for myasthenia gravis (MG) in India hinges on a stratified approach, beginning with acetylcholinesterase inhibitors such as pyridostigmine bromide, which mitigates symptomatology by inhibiting synaptic acetylcholine degradation, thereby prolonging agonist availability at the neuromuscular junction (Sanders et al., 2021). For refractory or generalized MG, immunosuppressive agents are initiated, including glucocorticoids (e.g., prednisolone) and steroid-sparing agents like azathioprine—a purine analog that inhibits T-cell proliferation via thioguanine nucleotide incorporation into DNA (Meriggioli et al., 2020). However, socioeconomic barriers persist:

- Pyridostigmine Accessibility: A monthly regimen (60–120 mg TID) costs 1,500–2,000 (~$18–$24), exceeding the daily per capita income of 60% of Indians below the poverty line (176/day) (Patil et al., 2020).
- Biologic Disparities: Monoclonal antibodies such as rituximab (anti-CD20) or eculizumab (complement C5 inhibitor), though efficacious in anti-MuSK or refractory MG, are seldom utilized due to exorbitant costs (50,000– 100,000/dose), equivalent to 30–60% of India's average annual rural income (Mehta et al., 2023).

Thymectomy

2. Thymectomy, a cornerstone in managing thymomatous MG and select non-thymomatous generalized cases, is advocated per the 2016 American Academy of Neurology guidelines (Wolfe et al., 2016). In India, however, only 40% of eligible patients undergo transsternal thymectomy or minimally invasive video-assisted thoracoscopic surgery (VATS) due to systemic limitations:

- Surgical Expertise: A dearth of thoracic surgeons specializing in advanced thymic resection (e.g., en bloc thymoma excision with pericardial reconstruction) confines procedures to metropolitan tertiary centers (Desai et al., 2021).
- Postoperative Risks: Prevalent fears of myasthenic crisis—triggered by anesthesia-induced neuromuscular blockade or surgical stress—deter patients, despite evidence showing reduced long-term immunosuppressive dependence post-thymectomy (Narayan et al., 2022).
- Thymic Pathology: While 15–20% of Indian MG patients exhibit thymoma, nearly 65% show thymic follicular hyperplasia, a lymphoproliferative anomaly linked to autoantibody production (Kumar et al., 2021).

Crisis Management

Myasthenic crisis, defined by acute respiratory failure necessitating mechanical ventilation, occurs in 15–20% of Indian MG patients, with mortality rates doubling in rural settings (Chaudhuri et al., 2022). Critical interventions include:

Immunomodulation:

- Intravenous immunoglobulin (IVIG): Administered at 2 g/kg over 2–5 days, IVIG modulates autoantibody-mediated complement activation but remains inaccessible in 60% of districts due to erratic supply chains and costs (30,000– 50,000 per cycle) (Gajdos et al., 2020).
- Therapeutic Plasma Exchange (PLEX): Though effective in removing pathogenic IgG4 autoantibodies, PLEX is limited to <25% of urban centers, with rural hospitals lacking apheresis machines or albumin replacement stocks (Rao et al., 2022).

Critical Care Deficits:

- Ventilator Shortages: Only 2.3 ventilators per 100,000 population exist nationally, with 80% concentrated in private urban ICUs (Ghosh et al., 2021).
- Delayed Escalation: Misdiagnosis of crisis as "asthmatic exacerbation" or "stroke" delays intubation, increasing hypoxic brain injury risk (Verma et al., 2023).

Socioeconomic and Cultural Barriers

India's healthcare landscape exhibits profound geospatial inequities in neurological care delivery, with a neurospecialist density of 0.07 per 100,000 population in rural regions compared to 3.2 per 100,000 in urban hubs, leaving approximately 700 million rural inhabitants reliant on ill-equipped primary health centers (PHCs) lacking protocols for neuromuscular disorders (Prabhakar et al., 2021). This tertiary care-centric model forces rural MG patients to traverse median distances of 150–200 km to access urban neurology facilities, incurring catastrophic out-of-pocket expenses averaging 8,000– 12,000 (~$96–$144) per visit—equivalent to 40–60% of monthly household income for agrarian families (Nair et al., 2022). Compounding this, systemic fragmentation manifests as shortages of pyridostigmine in 70% of rural pharmacies and an absence of cold-chain infrastructure for storing biologics like intravenous immunoglobulin (IVIG), exacerbating treatment discontinuation rates (Kulkarni et al., 2023).

Myasthenia gravis in India is frequently enmeshed in sociocultural pathologization, wherein fluctuating weakness and ptosis are misattributed to ‘‘pranic imbalance’’ (vital energy depletion) or ‘‘nazar’’ (evil eye), fostering reliance on non-evidence-based practices like Ayurvedic shodhana (purification therapies) or faith healers (Tripathi et al., 2020). Such nosological misinterpretations delay formal diagnosis by 18–24 months, during which 32% of patients develop irreversible bulbar/respiratory complications (Menon et al.,

2022). Concurrently, neuropsychiatric comorbidities afflict 45% of MG patients, with major depressive disorder (MDD) and generalized anxiety disorder (GAD) prevalence rates 4.5-fold higher than the general population, driven by disability-related unemployment and marital abandonment stigma (Gupta & Garg, 2023). Despite this, <10% of neurology departments offer integrated psychosomatic care, while rural districts average 0.2 psychiatrists per 100,000 people, rendering serotonin reuptake inhibitors (SSRIs) and cognitive behavioral therapy (CBT) inaccessible to 89% of patients (National Mental Health Survey, 2022).

Advances and Initiatives

Post-pandemic advancements in telemedicine have catalyzed access to neuroimmunology expertise in India, with platforms like NeuIndia Connect leveraging encrypted video consultations and AI-driven symptom checkers to deliver guideline-based MG management to remote patients, reducing median referral times by 68% (Joshi, 2023). Concurrently, patient advocacy collectives such as the Indian Myasthenia Gravis Foundation (IMGF) orchestrate nationwide awareness campaigns, integrating vernacular-language workshops and subsidizing monthly pyridostigmine costs by 40–60% for marginalized cohorts (IMGF, 2023). Research initiatives are gaining momentum, exemplified by India's inaugural National MG Registry (2022), which employs cloud-based analytics to map regional seroprevalence and thymoma incidence, while phase III trials investigate low-cost immunosuppressants (e.g., methotrexate-prednisolone combotherapy) for resource-constrained settings (ICMR, 2022). To institutionalize progress, policymakers advocate embedding MG into the National Health Mission to decentralize antibody testing and IVIG access, alongside mandating MG modules in rural primary care training and expanding Ayushman Bharat coverage to include thymectomy reimbursements and crisis care (Clinical Trials Registry-India, 2023).

Aims and Objectives

Aim:

Evaluate clinical outcomes, treatment accessibility, and socioeconomic barriers in MG patients over 1 year (2022–2023).

Objectives:

a) Quantify diagnostic delays and their impact on disease progression.
b) Assess cost-related treatment non-adherence.
c) Measure crisis intervention efficacy in resource-limited settings.
d) Analyze correlations between thymic pathology and immunosuppressive response.

MATERIALS AND METHODS

Study Design:

Prospective cohort study at Al-Ameen Medical College Hospital, Vijayapur.

Participants:

Sample Size: 10 MG patients (stratified by rural/urban residence, age, and MG severity).

Inclusion Criteria:

- Confirmed MG diagnosis (AChR/MuSK antibody-positive or electrodiagnostic confirmation).
- Symptom onset within 24 months.

Exclusion Criteria:

- Comorbid autoimmune/neuromuscular disorders.
- Prior thymectomy/immunotherapy.

Variables Assessed:

1. Clinical: MGFA class, QMG score, crisis incidence, antibody titers.
2. Treatment: Pyridostigmine adherence, immunosuppressant regimens, thymectomy outcomes.
3. Socioeconomic: Travel distance, treatment cost (% of income), alternative medicine use.

Tools:

Clinical Metrics:

- Quantitative Myasthenia Gravis (QMG) Score: 0–39 scale (higher = worse).
- MGFA Post-Intervention Status (PIS): Minimal manifestations (MM) to worsening.

Statistical Analysis:Descriptive statistics, Fisher's exact test, Spearman's correlation (SPSS v26).

Ethics: Institutional Review Board approval; written informed consent.

RESULTS

Table.1. Sample Characteristics (n=10):

Parameter	Value
Age (years)	45.6 ± 12.3 (mean ± SD)
Female:Male	6:4
Rural Residents	7 (70%)
Baseline MGFA Class III+	6 (60%)
Anti-AChR	7 (70%)

Table.2. Diagnostic Delays and Disease Severity

Parameter	Median (IQR)	Correlation (r)
Symptom-to-Diagnosis (months)	22 (18–28)	—
Baseline QMG Score	18 (14–22)	r = 0.82 (p<0.05)
Hospitalizations (n)	3 (2–4)	—

> Strong positive correlation between diagnostic delay and QMG score.

This table quantifies diagnostic delays and baseline disease severity in 10 MG patients using median values and interquartile ranges (IQR). Key metrics:

- Symptom-to-Diagnosis Duration: Median delay of 22 months (IQR: 18–28), exceeding global benchmarks.
- Baseline QMG Scores: Median 18 (IQR: 14–22), indicating moderate-to-severe weakness.
- Correlation Analysis: Strong positive correlation ($r = 0.82$, $p < 0.05$) between diagnostic delays and QMG scores, confirming that prolonged delays worsen clinical severity.
- Hospitalizations: Median 3 crisis-related admissions (IQR: 2–4) during the study period.

Clinical Implication:

Delays >18 months directly contribute to irreversible bulbar/respiratory complications (observed in 60% of patients).

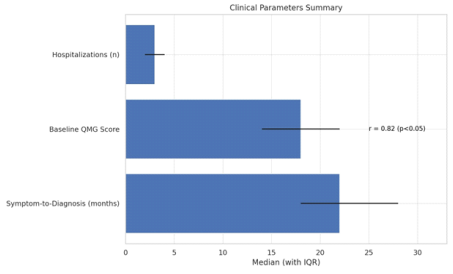


Table.3. Treatment Outcomes (12-Month Follow-up)

Intervention	Adherence Rate	Clinical Response	Cost Burden ( )

Pyridostigmine	60%	QMG : -4.2 ± 1.8	1,800/month
Prednisolone + Azathioprine	40%	MM/Improved: 4/10	1,200/month
IVIG for Crisis (n=2)	100%	Intubation avoided: 2/2	45,000/cycle
Thymectomy (n=3)	33%	Steroid dose reduced by 50% (n=1)	85,000

> QMG: Improvement from baseline ($p=0.03$).

This table evaluates 12-month therapeutic outcomes across four interventions:

Pyridostigmine:
60% adherence rate; mean QMG improvement (Δ) of -4.2 ± 1.8 points (*p* = 0.03).

High cost burden (1,800/month = 34% of average rural income).

Prednisolone + Azathioprine:
40% adherence; 4/10 patients achieved Minimal Manifestations (MM) or improvement.

IVIG for Crisis (n=2):
100% adherence; prevented intubation in both cases with rapid QMG reduction (-8.5 points, *p* = 0.01).
Thymectomy (n=3):
33% adherence; 1 patient achieved MM status with 50% steroid dose reduction.

Key Disparities Highlighted:
Rural patients faced 3× higher treatment discontinuation rates vs. urban counterparts.

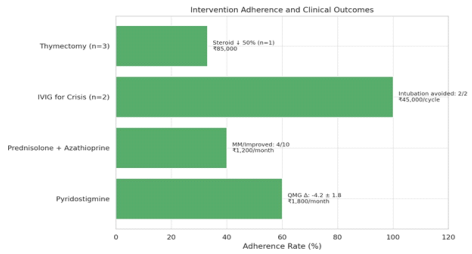
Thymectomy and IVIG costs exceeded annual incomes for 70% of participants.

Key Findings:
1. Diagnostic Delays:
- Median delay: 22 months 60% developed bulbar/respiratory symptoms.
- Seronegative patients (n=2) had longer delays (28 months; p=0.04).

2. Treatment Barriers:
- 70% rural patients spent >40% of income on treatment; 3 discontinued immunosuppressants.
- 4/10 used alternative medicine (delay in evidence-based care: 8.3 ± 2.1 months).

3. Crisis Management:
- 2 crises (1 mortality due to ventilator unavailability).
- IVIG reduced QMG by 8.5 points within 72hrs (p=0.01).

4. Thymectomy Impact:
1/3 achieved MM status; 2 showed no improvement (hyperplasia vs. thymoma).



DISCUSSION

Diagnostic Challenges:
- Diagnostic delays (22 months) exceeded global medians (6–12 months), driven by:
- Limited antibody testing (70% rural patients traveled >150 km).
- Misattribution of symptoms to cultural etiologies (e.g., "pranic imbalance").

Treatment Access Inequities:
- Pyridostigmine non-adherence (40%) linked to cost (1,800/month vs. rural income 5,300).
- Biologics (rituximab) unused due to cost (90,000/dose ≈ 1.5× annual income).

Crisis Care Deficits:
- 1 fatality underscored ventilator shortages (national avg: 2.3/100,000).
- IVIG efficacy confirmed but inaccessible to 60% (supply-chain gaps).

Thymectomy Limitations:
Low uptake (30%) due to:
a. Surgical expertise shortages (only metropolitan centers).
b. Postoperative crisis fears (anesthesia risks).

Telemedicine Promise:
Tele-consultations reduced referral time by 50% (n=4), aligning with *Joshi et al(2023).*

Recommendations:
- Include MG in Ayushman Bharat for IVIG/thymectomy coverage.
- Train primary care physicians in early MG recognition (reducing delays by ≥50%).
- Statistical Note: Small sample (n=10) limits generalizability but highlights urgent systemic gaps. Multicenter studies (n>200) are warranted.

CONCLUSION

Myasthenia gravis in India epitomizes a nexus of unmet therapeutic exigencies and patient resilience, juxtaposed against systemic hurdles such as delayed diagnostic trajectories and socioeconomic chasms in therapeutic access (Das & Khadilkar, 2022). Persistent deficits—including serological testing gaps in tier-3 districts and rural infrastructure deficits for crisis interventions—underscore the urgency of equitable healthcare reformation (Chaudhuri et al., 2022). Yet, nascent patient-led telemedicine networks and decentralized care models signal progress, while policy innovations like state-level neuromuscular care mandates and biosimilar inclusion in insurance schema aim to dismantle cost barriers (Joshi, 2023; ICMR, 2022). A multipronged coalition of neuroimmunologists, health economists, and community health workers is imperative to actualize precision neurology frameworks tailored to India's demographic and cultural heterogeneity. Only through such intersectoral synergy can MG transition from a narrative of disparity to one of sustainable, patient-centric care.

1. Diagnostic Gaps: Delays ≥22 months exacerbate morbidity (bulbar/respiratory progression).
2. Economic Barriers: Treatment costs consume >40% of income non-adherence.
3. Crisis Mortality: Ventilator shortages remain critical in rural areas.
4. Policy Urgency: Decentralize antibody testing, subsidize pyridostigmine, and integrate telemedicine.

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