Women and Myasthenia Gravis

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Abstract

Myasthenia gravis (MG) is a prototypical antibody-mediated autoimmune disorder of the neuromuscular junction, characterized by fluctuating skeletal muscle weakness and substantial morbidity. Although therapeutic advances have markedly improved survival and long-term outcomes, MG is not a gender-homogeneous condition. Women are disproportionately affected, exhibit a distinct bimodal age distribution, and experience the disease within unique biological and psychosocial contexts that shape presentation, disease course, quality of life, and treatment response. Accumulating evidence highlights sex-specific differences in immune reactivity, hormonal influences, thymic pathology, clinical severity, fatigue burden, and patient-reported outcomes. Notably, women consistently report poorer quality of life despite comparable disease severity. Reproductive health introduces additional complexity, as pregnancy planning, contraception, teratogenic risk, postpartum exacerbation, and neonatal complications profoundly influence clinical decision-making and patient autonomy. Despite these well-recognized disparities, sex-specific considerations remain insufficiently integrated into routine care and are strikingly underrepresented in clinical trial design. Most MG trials fail to stratify outcomes by sex, account for sex-dependent pharmacokinetics or pharmacodynamics, or include pregnancy-relevant populations, resulting in critical evidence gaps. This narrative review synthesizes current knowledge on gender-related pathophysiological mechanisms, clinical phenotypes, and life stage–specific management of MG, with particular emphasis on the reproductive years. It also briefly examines the evolving role of novel biological therapies, including complement inhibitors, neonatal Fc receptor inhibitors, and B-cell–directed agents, which offer promise for more targeted and potentially safer treatment paradigms. Systematic gender-stratified analyses, dedicated pregnancy registries, and proactive, physician-led counselling are essential to advancing equitable, evidence-based care for women living with MG.

Keywords: Myasthenia gravis, women, quality of life, pregnancy, neonatal myasthenia

Introduction

Myasthenia gravis (MG) is a classical antibody-mediated autoimmune disorder of the neuromuscular junction, characterized by fluctuating skeletal muscle weakness with potentially severe consequences. With advances in immunomodulatory therapies, outcomes for patients with MG (pwMG) have improved substantially compared with the early 20th century, when mortality rates were as high as 70%. As is typical of autoimmune disorders, MG demonstrates a marked gender bias, affecting women nearly three times more often than men. This is accompanied by a bimodal age distribution in women, with peaks in the third to fourth decades and again in the sixth decade. By contrast, men most commonly develop the disease later in life, earning MG the epithet of a "disease of young women and old men."[1] MG also demonstrates gender-related differences, suggesting that the disease may manifest, be experienced, and potentially respond to treatment differently between sexes. For example, a recent meta-analysis reported lower quality-of-life (QOL) scores among women despite adjustment for disease severity and age.[2] Despite these observations, sex-specific considerations in MG remain insufficiently emphasized. Importantly, gender disparities are inadequately addressed in clinical trial design. Most MG trials do not stratify outcomes by sex, account for sex-specific differences in pharmacokinetics or pharmacodynamics, or include subgroup analyses for differential efficacy and safety. Moreover, as pregnant women are systematically excluded from drug trials, a significant gap persists in evidence-based guidance for MG during pregnancy and across the reproductive lifespan. In this narrative review, we comprehensively examine gender-related aspects of MG, including sex-specific pathophysiological and clinical differences, disease course across the prepubertal, reproductive, pregnancy, postpartum, and menopausal stages, and the safety, efficacy, and practical considerations of immunotherapies across these phases.

A literature search was conducted to identify relevant publications addressing gender-specific issues in MG. Electronic databases, including PubMed/MEDLINE, Embase, and Google Scholar, were searched from inception until December 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms, including

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"myasthenia gravis," "women," "female," "gender differences," "pregnancy," "reproductive health," "fertility," "guidelines," and "recommendations," using Boolean operators ("AND," "OR") as appropriate.

Relevant clinical studies, review articles, consensus statements, and international guidelines addressing women-specific aspects of MG—such as pregnancy, fertility, contraception, and gender-related clinical considerations—were included. Additional studies were identified through manual screening of reference lists to ensure comprehensive coverage. Only articles published in English were considered.

Pathophysiology in Women

There is substantial evidence that gender-related pathophysiological differences contribute to the differential expression of autoimmune diseases between the sexes. These differences extend beyond prevalence to include variations in disease severity and clinical manifestation [Table 1]. Although sex hormones play a central role, the effects of estrogen have been proven to be contradictory, exerting both protective and pathogenic effects in female autoimmunity, indicating the involvement of multiple interrelated biological and environmental factors.[3] Women exhibit higher immune reactivity, which may provide advantages in immunocompetence but also increases the chance of autoimmunity.[4] Differences have also been observed in T helper 1 (Th1) and T helper 2 (Th2) responses, with Th-2-driven chronic autoantibody-mediated inflammation predominating in women.[5] In addition, women demonstrate higher expression of genes involved in toll-receptor (TLR) pathways and stronger type I interferon (IFN) responses. They also exhibit enhanced phagocytic activities of neutrophils and macrophages, more efficient antigen-presenting cell function, dysregulation of innate lymphoid cells, higher CD4/CD8 ratios, elevated basal immunoglobulin levels, and increased B-cell numbers, and lower regulatory T-cell (Treg) counts. Overall, elevated immune reactivity, differential target organ susceptibility, and the influence of hormonal changes across the entire reproductive cycle, along with environmental, genetic, and epigenetic factors, including X chromosome inactivation (XCI), contribute to sexual dimorphism in autoimmune disorders.[4,14] Specifically, in MG, skewed XCI patterns, where selective inactivation of X-linked self-tolerant immunological genes leading to autoimmunity, are more frequent in young women with MG compared with healthy controls.[15] Estrogens enhance Th2 and B-cell responses and influence thymic epithelial cell maturation, contributing to thymic hyperplasia, collectively increasing susceptibility to MG. In contrast, testosterone promotes thymic tolerance and suppresses T- and B-cell activity.[1]

Differences in the Clinical Features

Studies demonstrate a complex and heterogeneous influence of gender on various clinical aspects of MG. In general, MG tends to present with generalized symptoms at onset in females, whereas ocular symptoms predominate in males. This disparity is particularly evident in early-onset MG (EOMG), while the gender difference diminishes in late-onset MG (LOMG). Moreover, female sex has been associated with a slightly higher risk (odds ratio [OR] 1.06) of progression from ocular to generalized MG in a recent systematic review, although the quality of evidence was low.[16] Thymic follicular hyperplasia, which is associated with higher acetylcholine receptor (AChR) antibody levels, is significantly more common in females and may be one of the reasons behind early generalization.[17] Despite this, some studies point to a delay in the diagnosis of MG in women, although this finding has not been consistently reproduced.[18,19]. Another feature unique to women of reproductive age is the cyclical symptom exacerbation, which begins 2–3 days before menstruation and often persists the first three days of the cycle, sometimes requiring temporary medication increases. This occurs irrespective of antibody status, stress, oral contraceptive use, or type of MG therapy.[6] In addition, a consistent observation across studies is that the severity of the disease and lack of improvement with treatment based on both objective and subjective measures seem to be negatively favoring women.[19,20] Women tend to experience greater severity of MG and have a higher risk of refractory MG than their male counterparts.[21] Tasks related to personal grooming and family responsibilities, which are often more commonly undertaken by women, may be better reflected in questionnaires assessing activities of daily living, potentially resulting in poorer scores. The longer duration of disease in women with MG may also be another reason. A recent systematic review and meta-analysis of fifteen studies that examined the gender differences in QOL in pwMG revealed that women with MG experience a significantly lower QOL compared to men.[2]

Several psychosocial and biological factors likely contribute to this disparity. Among these, fatigue is a prominent syndrome of several neuromuscular disorders, and although the exact cause is unclear, it has a significant and multidirectional relationship with QOL.[22] Fatigue has been well documented as having a clear association with depressive symptoms, female sex, and disease severity. Women with MG experience greater fatigue, as well as disproportionately higher levels of anxiety and depression, which can contribute significantly to poorer QOL.[22] Misinterpretation of fatigue as a psychosomatic manifestation could also contribute to the delayed diagnosis of MG in women. In addition, a higher proportion of women have comorbid autoimmune disorders such as thyroid dysfunction, hemolytic anemia, and autoimmune hepatitis, which further increase disease burden.[12] Despite these observations, there is a paucity in the understanding of gender-related differences in MG. This gap has immense relevance not only in clinical practice but, more critically, in the setting of drug trials in MG.

MG in Prepuberal Age

The absence of a significant sex hormone influence results in a striking gender parity in the prepubertal period, evidenced by a 1:1 prevalence ratio and similar clinical phenotypes and therapeutic outcomes. Juvenile MG shares several common features with adult disease, including ocular predominance, higher rates of seronegativity, and a greater likelihood of spontaneous remission. However, prepubertal girls are slightly more prone to generalization than boys, although less so than adult women.[23]

MG in Reproductive Age

MG itself does not negatively impact fertility in either men or women. However, there might be factors such as coexisting autoimmune disorders, treatment choices, and psychosocial concerns about pregnancy that indirectly influence childbearing decisions. Among these, psychosocial concerns appear to be particularly significant as the diagnosis of MG plays a substantial role in influencing patients' reproductive decisions. A study examining family-planning choices among women with MG highlighted the magnitude of this impact and revealed several underlying concerns and misconceptions driven by limited knowledge that shape these decisions. Nearly 80% of women reported that MG influenced their decision to avoid pregnancy.[24] The most frequent concerns included the risk of drug-related teratogenicity, worsening of MG during pregnancy, passing MG on to offspring, and concern about weakness impeding delivery and child care. Other factors included older age, limited disease-related knowledge, longer disease duration, and prior negative personal experiences such as intensive-care treatment for MG.[24] A large majority of participants thought that their treating physicians should initiate discussions on

Table 1: Factors associated with increased disease activity or worsening of myasthenia gravis in women

Factor	Mechanism/Clinical basis	Clinical implication
Hormonal fluctuations (menstrual cycle)	Estrogen-mediated immune modulation; increased Th2 activity and B-cell responses[3-5]	Premenstrual worsening of symptoms reported in some women; may require temporary medication adjustment[6]
Early disease phase (first 2–3 years after onset)	Period of highest immunological activity and unstable disease course[7,8]	Higher likelihood of exacerbations and myasthenic crisis
Pregnancy-related immunological shifts	Altered immune tolerance and pharmacokinetic changes[7]	Variable course; ~30%–40% of patients experience worsening during pregnancy[7]
Postpartum immune rebound	Reversal of pregnancy-induced immune tolerance	Increased risk of disease exacerbation and new-onset MG in the first 6 months postpartum[9]
Active or poorly controlled disease	Higher MGFA class, elevated MGC score, abnormal repetitive nerve stimulation[10]	Increased risk of worsening during pregnancy or stressors
Infection and physiological stress	Increased metabolic demand and immune activation	Known triggers of exacerbation and myasthenic crisis[11]
Medication withdrawal or non-adherence	Sudden reduction of immunosuppression	Increased risk of relapse or exacerbation[8]
Coexisting autoimmune diseases	Shared autoimmune susceptibility (e.g., thyroid disease)[12]	Increased disease burden and potential worsening
Drugs that exacerbate myasthenia gravis (e.g., macrolides, magnesium)	Impaired neuromuscular transmission	May precipitate weakness or crisis[13]

MG: Myasthenia gravis, MGFA: Myasthenia gravis foundation of America, MGC: Myasthenia gravis composite

Table 2: Factors influencing optimal timing of conception in women with myasthenia gravis

Factor	Rationale	Clinical recommendation
Duration of MG	Disease activity highest in the first 2–3 years after onset[7,8]	Ideally, delay conception until disease stability achieved (≈2 years)
Disease stability	Active myasthenia gravis associated with worsening during pregnancy[7]	Aim for ≥6 months of stable disease or minimal manifestation status before conception
Pharmacological remission	Reflects adequate disease control	Preferably, before pregnancy when feasible
Thymectomy status	Associated with improved disease control and reduced exacerbations[26,27]	Pregnancy preferably ≥6–12 months after thymectomy[26]
Medication regimen	Some drugs are teratogenic (e.g., mycophenolate, methotrexate)[28]	Switch to pregnancy-compatible drugs before conception
Access to specialist care	Multidisciplinary management improves maternal–fetal outcomes[7,29]	Pregnancy ideally planned with neurologist–obstetrician collaboration
Maternal age and reproductive plans	Delayed conception may increase obstetric risks	Balance disease stability with reproductive timing
Previous pregnancy outcomes	Prior worsening or neonatal myasthenia gravis may influence risk assessment[7,30]	Requires individualized counseling before the next pregnancy

MG: Myasthenia gravis

Table 3: Safety of commonly used therapies for myasthenia gravis during pregnancy and lactation

Drug/Class	Pregnancy safety	Key considerations in pregnancy	Breastfeeding
Pyridostigmine	Generally safe	First-line symptomatic therapy; dose adjustments may be required due to altered pharmacokinetics during pregnancy[33]	Compatible
Corticosteroids (Prednisone/Prednisolone)	Generally safe	Most commonly used immunosuppressant in pregnancy; minimal fetal exposure due to placental metabolism; monitor maternal risks[34]	Compatible; minimal transfer into breast milk
Azathioprine	Acceptable when clinically indicated	Extensive data support relative safety[35,36]	Compatible with monitoring
Mycophenolate mofetil	Contraindicated	Strong teratogenic risk; discontinue ≥6 weeks before conception[28]	Contraindicated
Methotrexate	Contraindicated	Highly teratogenic; discontinue several months before conception[28]	Contraindicated
Cyclophosphamide	Contraindicated	Associated with fetal toxicity and miscarriage[28]	Contraindicated
Tacrolimus	Acceptable in selected cases	Possible risks of gestational diabetes and neonatal renal dysfunction; requires therapeutic drug monitoring[37]	Generally compatible
Cyclosporine	Acceptable in selected cases	No clear increase in congenital malformations; monitor maternal hypertension and renal function[38]	Generally compatible
Intravenous immunoglobulin	Safe	Used for exacerbations or myasthenic crisis[11]	Compatible
Plasma exchange	Safe when indicated	Requires careful monitoring of maternal hemodynamics and electrolytes[11,39]	Not applicable
Rituximab	Limited but increasing safety data	Possible neonatal B-cell depletion; ideally avoid conception for several months after infusion[40,41]	Minimal transfer; generally compatible
Complement inhibitors (e.g., eculizumab)	Limited data	Emerging evidence suggests possible safety but insufficient myasthenia gravis-specific data[42-44]	Limited data
FcRn inhibitors (e.g., efgartigimod, nipocalimab)	Insufficient evidence	Not currently recommended during pregnancy; ongoing studies evaluating safety[42-44]	Unknown

FcRn: Neonatal Fc receptor

family planning and that the provision of information is a major determinant of decision-making. However, these findings cannot be readily generalized, as regional, ethnic, and cultural contexts inevitably shape reproductive decision-making. In India, in particular, these concerns may be more nuanced and complex. There is a knowledge gap with very little data in the Indian context. Contributing factors particular to the Indian context may include insufficient time during consultations, hesitation in openly discussing reproductive health issues, social and familial stigma, limited access to specialists, and perceived or actual lack of support from family or partners.[25] Therefore, a discussion on reproductive health should begin ideally at the first consultation and be tailored to each patient's needs, health literacy, and disease understanding. Counseling should ideally cover fertility and contraception, medication options with their associated precautions and adverse effects, and optimal timing of thymectomy and conception, while continuously encouraging patients to voice any concerns and questions at each visit. Follow-up sessions may subsequently detail further pregnancy-related considerations and relevant precautions. The involvement of partners or family members may be encouraged, while ensuring the patient's autonomy and preferences.

Timing of Pregnancy

Women of reproductive age with MG and their caregivers are often faced with the dilemma of deciding the ideal time for conception, particularly in primigravidas. On one hand, there is the risk of disease exacerbation, while on the other hand are the couples' personal preferences and concerns related to advancing maternal age. Although definitive recommendations are not available, evidence from patient cohorts and systematic reviews suggests several influencing factors. These include disease duration, severity, and stability, thymectomy status, drug continuation, and access to specialized care; the impact of these factors is inconsistent [Table 2].[7] Several studies suggest that a minimum interval of two years between disease onset and pregnancy may be desirable, with some reporting a threefold increase in the risk of worsening when conception occurs earlier.[8] This recommendation reflects the natural history of MG as disease activity is typically highest during the first two or three years, with the highest chance of MG crisis and has a low likelihood of achieving pharmacological remission. Thymectomy, which is generally deferred until the patient's disease is relatively stabilized, and the subsequent time required for antibody decline, along with the delayed onset of action of commonly employed steroid–sparing agents such as azathioprine, further supports avoiding pregnancy in the first two years. A minimum duration of 6–12 months after thymectomy is generally recommended and is considered one of the strongest factors alleviating the risk of worsening.[26] Disease severity, measured in terms of the MG composite (MGC) score and findings such as abnormal repetitive nerve stimulation indicating suboptimal disease control, is also an important factor.[10] Ideally, a period of at least 6 months of pharmacological remission or "stable disease" with minimal doses of medications or minimal manifestation status (as per myasthenia gravis post-intervention status [MGFA PIS] classification) may serve as a practical benchmark. At the same time, abrupt

discontinuation of medications, especially corticosteroids or azathioprine, just before or during pregnancy has been associated with disease worsening.[8] Because of these complexities, women with MG who are pregnant or planning pregnancy are best managed in specialized centers with the expertise of neurologists and obstetricians experienced in caring for high-risk pregnancies. However, such access may be limited in resource-limited settings like ours.

Timing of Thymectomy

There is sufficient data to recommend thymectomy in adults younger than 60 years with non-muscle-specific kinase (MuSK) generalized MG.[27] Prior thymectomy is associated with nearly a fivefold greater likelihood of improved outcomes during pregnancy, along with a significantly lower risk of disease worsening.[26] In addition, neonates born to mothers who have undergone thymectomy have approximately half the risk of developing neonatal MG, probably due to reduced AChR antibodies.[26] Elective thymectomy is not recommended during pregnancy as it does not facilitate rapid relief of MG symptoms and exposes the patient to surgery-related complications. An exception may be made in case of malignant or invasive thymoma, where its neoplastic nature may threaten the mother's survival. In such cases, a joint decision involving the neurologist, oncologist, obstetrician, and neonatologist is required, with consideration given to the patient's informed preferences.

Contraceptive Use in MG

As part of reproductive counseling, particularly in newly diagnosed patients, it is essential to proactively address contraception. Apart from anecdotal reports of symptom worsening during the cyclical withdrawal phase of combined oral contraceptive pills (OCPs), there is limited evidence to guide the choice between different contraceptive methods. Both combined OCPs and intrauterine devices are generally considered safe in MG, and the choice is left to the patient in consultation with the gynecologist. One important concern is the concurrent use of estrogen-containing OCPs with tacrolimus, as the estrogen can increase tacrolimus blood levels, raising the risk of drug toxicity. In such cases, closer monitoring of trough concentrations is recommended.[31]

Drugs and Teratogenicity

Teratogenicity is a major source of concern for many couples and remains an important reason for delaying pregnancy in MG. It may also contribute to medication nonadherence among women attempting to conceive, with potentially serious consequences. Although the U.S. Food and Drug Administration (FDA) replaced the traditional pregnancy risk categories with the Pregnancy and Lactation Labeling Rule (PLLR) in 2015, the A, B, C, D, and X classification system continues to be widely used in clinical practice.[32] Accordingly, mycophenolate mofetil (Schedule D), cyclophosphamide (Schedule D), and methotrexate (Schedule X) are not prescribed for women planning pregnancy and should be discontinued at least 6 weeks before conception.[28] Table 3 summarises the safety profile of the commonly used MG drugs in pregnancy and lactation.

Azathioprine (AZA): FDA has scheduled AZA as a pregnancy category D drug; however, clinical evidence and meta-analyses consistently demonstrate its safety in autoimmune diseases, including MG. Although AZA and its active metabolite 6-thioguanine nucleotide (6-TGN) cross the placenta, fetal/neonatal exposure is substantially lower. Large meta-analyses found no increase in congenital malformations or low birth weight, with any observed differences diminishing when compared with disease-matched controls not receiving thiopurines.[35] The slight increase in preterm birth (adjusted OR 2.4–4.9 in some studies) is largely attributable to underlying maternal illness rather than the drug itself. Recent prospective cohorts have confirmed no increase in miscarriage, congenital malformations, intrauterine growth restriction, or developmental delay. Long-term follow-up shows no excess infections, immunodeficiency, or neurodevelopmental abnormalities.

Cyclosporine A (CsA) and tacrolimus (TAC): CsA and TAC are calcineurin inhibitors used as second-line immunosuppressants in refractory MG. Emerging evidence supports their efficacy in reducing myasthenic exacerbations and steroid doses. Although most pregnancy safety data come from transplant recipients, these findings can be cautiously extrapolated to MG.[38] Systematic reviews and meta-analyses confirm no increased risk of congenital malformations with either agent, which aligns with FDA pregnancy category C labeling.[37,38] Observed associations with preterm birth (rates 20%–40%, OR 1.5–2.5) and low birth weight are primarily confounded by underlying maternal disease activity or comorbidities rather than direct drug effects. CsA exposure is correlated with higher maternal eclampsia risks, whereas TAC is linked to gestational diabetes and rare neonatal transient renal dysfunction or hyperkalemia. In MG, small series report uneventful outcomes with stable dosing, emphasizing preconception optimization and therapeutic drug monitoring to minimize toxicity. For lactation, data from both exposures indicate minimal infant exposure, with no adverse neurodevelopmental or infectious sequelae observed during follow-up periods of 2–3 years. The EULAR guidelines endorse continuing stable CsA/TAC regimens during pregnancy for indicated MG cases, with level monitoring.[45] Overall, CsA and TAC offer a favorable risk–benefit ratio in MG pregnancies when alternatives fail.

Steroids: Corticosteroids remain the most commonly used immunosuppressants in pregnant pwMG and are considered safe during pregnancy. Recent systematic reviews report no consistent teratogenic signals and confirm their safety, although older data suggested a small increased risk of orofacial clefts with first-trimester exposure.[34] The typical maintenance dose during pregnancy ranges from 5 mg to 20 mg per day. The

principal concerns are maternal, such as gestational diabetes, hypertension, weight gain, and bone demineralization; therefore, the dosage is maintained at the lowest possible level, adjusted during the period leading to conception. For breastfeeding, prednisolone is considered compatible as only very small quantities pass into breast milk. Additionally, a 2–4 hour delay after high oral doses can further minimize infant exposure.

Intravenous immunoglobulin (IVIG) and plasma exchange (PLEX): Both IVIG and PLEX are generally reserved for managing MG exacerbations and crises during pregnancy; however, some centers occasionally use them as maintenance therapy when other options fail.[11] The main concerns include volume overload, increased plasma viscosity, and the risk of thromboembolic events during pregnancy, requiring a patient-specific approach. The physiological plasma volume expansion during pregnancy (approximately +6% in the first trimester, ~30% by mid-pregnancy, and 45%–50% near term) has direct implications, especially for calculating the volume of PLEX.[39] The dosage for IVIG remains the same, but slower infusion rates and adequate hydration are essential. Subcutaneous IVIG offers several advantages, including lower and more sustained immunoglobulin levels and a reduced chance of fluid overload. However, it may not be ideal in the Indian context due to costs and logistics in setting up the infusion.[46] For PLEX, a more frequent lower-volume sessions (0.8–1 plasma volume) during the second and third trimesters, particularly in patients with anemia or hemodynamic fragility, are preferable to avoid maternal hypotension and uteroplacental hypoperfusion. Citrate anticoagulation is safe but requires monitoring for hypocalcemia, which should be treated promptly with calcium infusion.

Pyridostigmine: Pyridostigmine is safely used throughout conception, pregnancy, delivery, and lactation. Large reviews of MG in pregnancy indicate no teratogenic side effects attributable to pyridostigmine.[33] Physiological changes during pregnancy may necessitate dose increases, which should be titrated based on patient symptoms. Monitoring for cholinergic symptoms is essential as there are rare reports of increased uterine tone late in pregnancy, suggesting caution at higher cumulative doses. Pyridostigmine should be continued during delivery and is considered fully compatible with breastfeeding; milk transfer is minimal, and infant serum levels are negligible.

Novel biologicals in pregnancy: The past decade has seen the rapid emergence of several classes of novel biological agents, such as complement inhibitors, neonatal Fc receptor (FcRn) inhibitors, and direct and indirect B-cell inhibitors, all of which offer significant advantages over conventional agents.[42-44] Although safety signals indicate no major adverse effects, none of these drugs is currently approved for use during pregnancy or lactation. Nipocalimab, the FcRn receptor inhibitor, deserves special mention as it has the least transplacental transfer and is the most likely to receive approval for use during pregnancy.[44] Rituximab (RTX), although not approved for the treatment of AChR-positive MG, has accumulated substantial real-world data suggesting its efficacy and safety in generalized MG.[44] Rituximab is classified as a category C agent and is increasingly used in women of reproductive age. The manufacturer recommends a washout period of 6–12 months before conception; however, accumulating evidence suggests that RTX is safe before pregnancy.[40,41] Rituximab and other monoclonal antibodies are large molecules that do not cross the placenta in the first trimester, making the risk of teratogenicity unlikely. During the second and third trimesters, transplacental transfer can result in neonatal B-cell lymphopenia, which requires monitoring, but no increased risk of infection has been observed. As the postpartum period poses a particularly high risk, the mother can be restarted on RTX 1–2 months post-delivery or earlier in high-risk cases. Because the expression of RTX in breast milk is negligible, there is no contraindication to breastfeeding.

During Pregnancy

A planned pregnancy with a well-coordinated and communicative multidisciplinary team is the desirable standard of care. Physiological changes during pregnancy, such as increased plasma volume leading to potential drug dilution, variable or reduced drug absorption, diaphragmatic elevation, and alterations in pharmacokinetics and pharmacodynamics across trimesters, must be carefully considered. However, pre-emptive dose adjustments are not routinely recommended; medication changes should be guided by the patient's clinical symptoms and disease activity. At times, it may be difficult to distinguish fatigue from MG from the physiological changes during pregnancy, which can also lead to fatigue. While subjective symptoms should be taken seriously, clinical parameters measured by physicians should also be prioritized before making therapeutic modifications. There is limited data regarding the course of ocular MG during pregnancy. However, anecdotal reports suggest that transient neonatal myasthenia gravis (TNMG) may occur in infants born to mothers with ocular MG. The risk of generalization may be higher in the postpartum period. As corticosteroids have been shown to reduce the risk of generalization, the continuation of low-dose steroids during pregnancy may be considered, although such decisions should be individualized and made on a case-by-case basis.[47]

Worsening symptoms during pregnancy should be promptly managed, and potential triggers such as urinary tract infections, thyroid dysfunctions, and treatment noncompliance should be actively investigated. Patients who continue to worsen despite an increase in steroids or are in an impending crisis should be admitted, and IVIG or PLEX should be initiated. The obstetrician and neonatologist should be involved to ensure the fetus's well-being and to make decisions regarding the termination of pregnancy based on its progression. Equal caution should be maintained while prescribing medications where antibiotics such as

macrolides and, particularly, magnesium, can have serious consequences.[13] In addition to the routine obstetrical precautions and periodic ultrasound scans recommended during pregnancy, the neurologist should inform both the patient and the obstetrician about the risk of autoimmune arthrogryposis multiplex congenita (AMC) due to the passive transfer of maternal antibodies against the gamma subunit of the fetal AChR subunit. Young mothers should be encouraged to monitor fetal movements and signs of AMC, which can be identified early during second-trimester ultrasounds, such as decreased mobility, flexion deformities, and scoliosis; however, these may be difficult to diagnose.[48] According to expert opinion, mothers with a previous history of AMC may be offered IVIG or PLEX at 12–14 weeks to reduce the risk, as discussed further below.

Delivery

Current evidence and consensus recommendations consistently support spontaneous vaginal delivery as the preferred mode of childbirth for women with MG, and caesarean section is indicated only when there are compelling maternal or fetal reasons.[11,29] Being composed of smooth muscle, the uterine muscles are unaffected by AChR antibodies and are not involved in MG. In patients who are in clinical or pharmacological remission, the normal progression of labor should be monitored carefully. Because oral absorption may be delayed or erratic, symptomatic patients may be switched to intramuscular neostigmine if needed. As labor progresses, patients should be closely monitored for signs of fatigability that could limit maternal effort; assistance with forceps or vacuum extraction should be used as appropriate.[11] If a caesarean section is required, regional anesthesia is preferred to general anesthesia, and the use of neuromuscular blocking agents should be avoided.

Postpartum

The postpartum period is arguably the most vulnerable time in a woman's life regarding the worsening of pre-existing MG and the potential onset of the disease. Epidemiological data show that the relative risk of MG onset rises nearly fivefold during the first six months after delivery, before returning to baseline over the subsequent six months.[9] This heightened susceptibility is most pronounced after the first childbirth and mirrors postpartum flare patterns observed in other autoimmune diseases such as rheumatoid arthritis and multiple sclerosis. A combination of hormonal shifts, immune rebound phenomena, physical and emotional stressors, and increased susceptibility to infections is believed to contribute to this increased risk. Therefore, both patients and physicians need to be extra vigilant for any early signs of worsening, emphasizing the importance of drug compliance; however, preemptive dose escalation is seldom warranted. Patients who have not been on RTX maintenance before or during pregnancy may be reinitiated early during this period, as breast milk secretion is negligible.

Transient Neonatal Myasthenia Gravis

TNMG occurs due to the transplacental FcRn-mediated transfer of maternal IgG antibodies directed against AChR, or infrequently against MuSK, resulting in post-synaptic receptor dysfunction in the neonate.[30] The incidence of TNMG is approximately 10%– 20% among infants born to myasthenic mothers. It manifests as a floppy infant in the first 1–2 days of life, characterized by generalized hypotonia, weak cry, poor suckling, and respiratory distress, with ptosis and ophthalmoplegia being unusual. Maternal disease severity is not a strong predictor of TNMG, and even asymptomatic mothers can lead to diagnostic confusion. A previous history of TNMG and anti-MuSK MG can indicate a more severe form of TNMG. Although often self-limiting and not lasting more than 4 months, the neonate may require a short course of pyridostigmine (1–4 mg/kg/day), and in severe cases, may require IVIG or PLEX.

On the other end of the spectrum of maternal autoimmune MG manifesting in the offspring is the more severe and irreversible fetal acetylcholine receptor inactivation syndrome (FARIS), which is the predominant autoimmune cause of AMC.[49] While in TNMG, the neuromuscular blockade is due to maternal IgG directed against the alpha epitope shared by fetal and adult receptors and is transient; FARIS is mediated by maternal antibodies directed against uniquely fetal gamma epitopes of the AChR. Placental transfer of these antibodies sharply increases from 16–20 weeks of gestation, coinciding with the critical developmental window for fetal movement, joint formation, and pulmonary growth. This results in fetal hypokinesia, joint contracture, pulmonary hypoplasia, and polyhydramnios. Unlike TNMG, prevention of FARIS in future pregnancies may warrant maternal IVIG or PLEX therapies during 12 to 14 weeks of gestation.[50]

MG in Menopause

With the diminishing influence of reproductive hormones, the sex distribution of MG once again reverses, revealing a clear male predominance in the fifth and sixth decades of life. As individuals age, they often face a host of comorbidities that can influence treatment decisions, although these comorbidities seldom have a significant impact on the disease itself.[51] Late-onset MG is usually characterized by a higher likelihood of seronegativity, a higher chance of generalization, and a greater likelihood of thymoma. Caution is warranted with hormone replacement therapy, because it has the potential to exacerbate autoimmune conditions, including MG, although current evidence remains limited and does not constitute a contraindication.

Special Considerations in the Indian Scenario

The management of MG in women in India occurs within a complex sociocultural and health-system landscape that

presents gender-specific challenges. India's large and geographically diverse population continues to experience significant disparities in access to neurological care. Neurologists are concentrated in urban tertiary centers, whereas a substantial proportion of the population resides in rural or semi-urban areas, creating barriers to timely diagnosis and access to specialized care. Women may face additional obstacles related to sociocultural norms that limit independent healthcare seeking, reliance on family members for travel to distant hospitals, and competing household responsibilities, all of which can contribute to delays in evaluation and continuity of care. Particularly significant are the reproductive health considerations intertwined with cultural expectations surrounding marriage and childbearing, as well as misinformation regarding fertility, pregnancy safety, and the potential hereditary nature of the disease, and the anxiety and stigma associated with medications. These factors often lead to medication compliance issues, which can have disastrous consequences. Limited preconception counseling further compounds uncertainty, potentially leading some women to postpone or avoid pregnancy despite the possibility of favorable outcomes. Financial constraints further influence treatment access. Although there have been advances in MG management globally, these treatments remain expensive and often inaccessible to many patients in low- and middle-income settings. In India, out-of-pocket healthcare expenditure remains high, and insurance schemes primarily prioritize acute hospitalizations rather than the long-term management of chronic neuromuscular diseases. Consequently, many women encounter difficulties accessing advanced therapies or sustained follow-up at specialized neuromuscular centers. Family structures in India can serve as both a challenge and a support. While sociocultural expectations may impose additional caregiving roles on women with chronic illness, extended family networks can also provide important practical and emotional support, facilitating treatment adherence and assistance with childcare or household responsibilities. Recognizing these context-specific challenges is essential for developing culturally and geographically sensitive care pathways, strengthening patient education, and enhancing physician perspectives in this setting.

Conclusions

Women with MG face a distinctive and often underappreciated set of challenges that extend beyond disease prevalence alone. Across the lifespan, fluctuating hormonal environments, higher immune reactivity, and sex-specific pathophysiological mechanisms influence disease onset, severity, and treatment response. These challenges are further magnified during the reproductive years. Despite these complexities, the underlying message is that the majority of women can conceive and can expect a normal pregnancy and delivery. Central to this is a well-planned, proactive, and multidisciplinary approach that begins well before pregnancy and evolves over time. The lack of insightful data and substantial gaps in knowledge are highlighted by the absence of a gender-specific stratification of outcome measures in clinical trials. Multicentric MG registries, especially those focused on pregnancy outcomes, are urgently needed, together with strengthened patient advocacy initiatives. Finally, the treating physicians play a pivotal role in driving these efforts and in maintaining longitudinal, life-stage–appropriate dialogue with women living with MG. The emergence of newer biological agents offers hope by potentially providing safer and more effective options, but further data must be gathered before using them during pregnancy.

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Conflicts of interest

There are no conflicts of interest.

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