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Risk of Myasthenia Gravis Exacerbation During Pregnancy and Postpartum

A Nationwide Cohort Study

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Abstract

Background and Objectives

The impact of pregnancy on the clinical course of myasthenia gravis (MG) remains uncertain, with existing evidence mainly derived from small case series. Using nationwide longitudinal register data, we aimed to assess the risk of MG exacerbation during pregnancy and up to 1 year postpartum.

Methods

In this population-based cohort study, we included women with MG recorded in the Swedish National MG Register who had singleton pregnancies documented in the Medical Birth Register after MG diagnosis (1987–2019). The exposure was pregnancy, and the outcome was MG exacerbation. The primary outcome measure was hospital admissions with MG during pregnancy and the postpartum year, compared with the year preceding pregnancy. Cox proportional hazards models estimated hazard ratios (HRs), adjusting for disease duration and prior thymectomy. The secondary outcome measure was changes in immunosuppressive MG medications during pregnancy and postpartum.

Results

We identified 112 women with MG (median age 30 years) with 176 singleton pregnancies. During pregnancy, women were not more likely to be hospitalized for MG than in the prepregnancy year (HR 0.74, 95% CI 0.39–1.41), and there was no increased risk of longer hospital admissions (HR 0.83, 95% CI 0.36–1.88). The postpartum period was associated with an increased risk of prolonged MG admissions during the first 3 months (HR 5.02, 95% CI 1.66–15.24), with a similar risk observed throughout the first 12 months postpartum (HR 4.52, 95% CI 1.26–16.14). During pregnancy, immunosuppressive MG medications were reduced or discontinued in 13 pregnancies and increased in 6. Postpartum, medications were initiated or escalated in 10 pregnancies and reduced in none. The risk of prolonged MG admissions was higher in periods outside of pregnancy compared with the prepregnancy year (HR 2.95, 95% CI 0.84–10.43), suggesting that women conceive during periods of relative disease stability.

Discussion

Pregnancy was not associated with an increased risk of MG exacerbation. The postpartum period was linked to more severe or prolonged exacerbations in a minority of women, highlighting the importance of close monitoring after delivery. Milder exacerbations not requiring hospitalization or clear medication escalation may have been underestimated, underscoring the need for larger prospective international studies that include detailed clinical data.

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Glossary

AChR = acetylcholine receptor; **ATC** = anatomical therapeutic chemical; **HR** = hazard ratio; **ICD** = International Classification of Disease; **MG** = myasthenia gravis; **MGFA** = Myasthenia Gravis Foundation of America; **MuSK** = muscle-specific kinase.

Introduction

Pregnancy represents a major life event and an important consideration for women of childbearing age living with myasthenia gravis (MG). As MG often manifests in early adulthood, reproductive decisions are frequently influenced by concerns about disease management. In a large cross-sectional study, 38% of women with MG reported choosing not to have children, with an additional 8% refraining due to partner-related reasons.[1] Fear of MG exacerbation during pregnancy was among the most frequently cited reasons for hesitation, expressed by approximately 70% of women.[2] These concerns highlight the broader impact of MG, not only on physical health but also on reproductive decision making and quality of life.

Clinically, MG is an autoimmune disorder characterized by fluctuating skeletal muscle weakness and variable disease activity. Whether pregnancy itself increases the risk of MG exacerbation remains uncertain. Although most studies suggest that planned pregnancies are generally safe, the literature presents somewhat conflicting evidence. Some reports describe stable or even improved clinical disease courses, whereas others indicate increased exacerbation rates, particularly in the postpartum period.[3-7] However, several of these studies are limited by small sample sizes, retrospective designs, and inconsistent definitions of exacerbation.

A meta-analysis of 15 studies estimated that 36% of women experienced worsening of MG and 28% reported improvement during or after pregnancy. The analysis revealed a publication bias toward studies reporting deterioration and suggested that the actual rate of worsening was likely closer to 19%.[8] There remains a lack of prospective and systematically collected data on the course of MG throughout pregnancy and the postpartum period. This knowledge gap complicates clinical counseling of patients and may contribute to unnecessary anxiety or avoidance of pregnancy among women with MG. Further evidence is required to guide clinicians and support women with MG in making informed reproductive choices.

To address these uncertainties, this study aimed to investigate the risk of MG exacerbation during pregnancy and up to 1 year postpartum, using nationwide longitudinal register data.

Methods

Study Population

Criteria for inclusion in the study were having had a singleton pregnancy recorded in the Medical Birth Register after MG diagnosis between 1987 and 2019. The women with MG were identified in the MG register, and their pregnancies were identified in the Medical Birth Register. Identification of study participants was possible due to the unique personal identification number assigned to all Swedish residents, which allows for individual-level linkage across registers.

Participants were identified by linking Sweden's national MG register with the Medical Birth Register, selecting all pregnancies recorded after MG diagnosis between 1987 and 2019. Only singleton pregnancies occurring after MG diagnosis were included.

Outcomes

The primary outcome was MG exacerbation, defined as the rate and duration of hospital admissions with MG recorded as the primary diagnosis or as any diagnosis. The secondary outcome was changes in immunosuppressive MG medications during pregnancy and up to 1 year postpartum.

Study Design and Register Linkage

Data for this study were obtained through linkage of multiple nationwide Swedish health registers, as summarized in eFigure 1.

1. Swedish MG Register: Established in 2001 through collaboration among Swedish neurology clinics, with regional coverage reaching approximately 83% in the Stockholm region.[9] The register aims for nationwide coverage and currently includes patients from at least 13 neurology clinics. It captures approximately 60% of all MG patients in Sweden, with higher representation among newly diagnosed patients. The register contains detailed longitudinal data on MG severity, treatment, and clinical subgroups. For patients diagnosed before its inception, retrospective data entry was performed at several centers. For this study, data were extracted for all 112 women with MG from the earliest available records.
2. Swedish Medical Birth Register: Established in 1973, this register captures 98% of all births in Sweden, including all live births and stillbirths reaching at least gestational week 22 + 0 (before 2008 reaching at least week 28 + 0). Data are entered prospectively and include pregnancy and delivery complications, as well as maternal and neonatal outcomes, and are coded according to the International Classification of Diseases (ICDs). All singleton pregnancies occurring after MG diagnosis between 1987 and 2019 were included.
3. Swedish National Patient Register (Inpatient and Outpatient): These registers provided information on hospital admissions (since 1987) and specialist outpatient visits (since 2001), including ICD coded

diagnoses 1 year before, during, and up to 1 year postpartum.
4. Swedish Cause of Death Register: Established in 1960 and updated annually, this register was used to identify mortality data.
5. Statistics Sweden: Supplied demographic data, including country of birth.

Data Sources: MG Subgroup and Disease Severity

The date of MG onset was defined as the earliest recorded MG diagnosis in the MG Register, Inpatient Register, or Outpatient Register. Disease duration was calculated from the date of formal diagnosis as documented in these registers.

Disease severity was assessed using the Myasthenia Gravis Foundation of America (MGFA) clinical classification recorded in the MG register. For each woman, 2 time points were considered: (1) the highest MGFA class ever documented, reflecting maximum disease severity, and (2) the MGFA class closest in time to pregnancy. When the MGFA class was not explicitly recorded, it was derived from available Quantitative MG or MG composite scores. In total, the MGFA class was available for 84 women (75%). Clinical severity scores were documented within 1 year of pregnancy for 56 pregnancies (32%). In 37 pregnancies (21%), these scores were recorded at least once during pregnancy itself. Owing to this limited temporal coverage, severity data were used to provide an overall characterization of disease severity rather than to assess dynamic changes during pregnancy.

Information on thymectomy was retrieved from the Inpatient Register using surgical procedure codes (KVÅ codes beginning with GEC and 0941, 0942, 0943, and 0949) and cross-referenced with the MG Register data. Additional clinical variables, including thymic histopathology, neurophysiology results, and level of hospital care (tertiary vs regional), were extracted from the MG Register.

Serologic data were obtained from the MG Register and supplemented with results from acetylcholine receptor (AChR) and muscle-specific kinase (MuSK) antibody radioimmunoassays performed at Karolinska University Hospital (available from 2007, with some historical data dating back to 1974) and Sahlgrenska University Hospital (available from 1999). MuSK antibody testing was routinely introduced in 2013.

Data Sources: Demographic and Pregnancy Data

Maternal age at delivery, parity, date of delivery, and gestational length at delivery were obtained from the Medical Birth Register. Country of birth was retrieved from Statistics Sweden.

Data Sources: Hospital Admissions and Outpatient Visits

We analyzed 459 inpatient admissions occurring in the peripartum period (1 year before, during, and up to 1 year after pregnancy) in the 112 women. For each admission, obtained data included all primary and secondary ICD diagnoses as well intervention codes (KVÅ), which include surgical procedures, therapeutic interventions, and administration of IV medications. From the Outpatient Register, 1,725 specialist outpatient visits during the peripartum period were identified in 89 women, including ICD-coded diagnoses, KVÅ intervention codes, and records of nonvisit contacts (telephone, letters, and follow-up of laboratory or diagnostic test results).

In addition, 697 inpatient admissions and 1,800 outpatient visits outside the pregnancy period were analyzed for MG-coded diagnoses (ICD-10 G70.0, ICD-9 358.0).

Data Sources: Medication Data

Data on MG medication use during the peripartum period were available for 163 of 176 pregnancies (93%) from 3 sources.

1. Prescribed Drug Register (from 2005): Complete data on dispensed oral medications were available for 108 pregnancies (61%) occurring after the register's inception. This register captures all outpatient prescriptions dispensed at pharmacies, recorded using Anatomical Therapeutic Chemical (ATC) classification codes, along with dispensing date, number of packages, and defined daily doses.
2. Swedish Medical Birth Register (from 1995): Among 149 pregnancies after the register's establishment, medication data were recorded for 51 pregnancies (34%). This register documents oral and IV medications administered during pregnancy using ATC codes; however, dosage information is not available. For pregnancies without recorded medications, it was not possible to determine whether the absence reflected true nonuse or missing data.
3. Swedish MG Register: Provided detailed data on MG-specific oral and IV medications in the peripartal period for 81 pregnancies (46%). This included drug names, start and end dates, dosages, and reasons for treatment discontinuation. The register also contains longitudinal data on all MG-related medications used since MG diagnosis for all 112 women, including clinical trial drugs and reported adverse effects. In 5% of pregnancies, the medication fields were blank, suggesting missing data.

Data on IV immunoglobulin (IVIG), rituximab, and plasmapheresis treatments were identified through the MG Register and the National Inpatient and Outpatient Registers. These therapies were captured using relevant KVÅ procedure codes for IV medication administration, immunotherapy, and plasmapheresis (DT016, DV033, DR006) and were included only when MG was listed as the primary diagnosis.

Remission was defined as the absence of MG medications recorded during pregnancy despite the pregnancy appearing in the medication registers. Beta-agonist use was noted, but it was not possible to distinguish between MG-related and non-MG indications.

Statistical Analysis

Cox regression with recurrent events was used to compare hospital admissions with MG in 3 time categories: the year before pregnancy (reference level), during pregnancy, and the postpartum period, providing the effect estimates hazard ratio (HR) and CI for the risk of MG exacerbation. The outcomes were (1) admissions with MG diagnosis and (2) nights in hospital with MG diagnosis. The analysis was performed for (1) admissions with MG as the primary diagnosis and (2) admissions with MG as any diagnosis. Postpartum period was defined as (1) the full year after delivery and (2) the first 3 months after delivery, which is the classic "postpartum" period.

Admissions for delivery, thymectomy, and day-case procedures (e.g., IV treatments) were excluded. For the Cox regression where MG was the primary diagnosis only admissions where MG was the primary diagnosis were included across the 3 time categories: prepregnancy, pregnancy, and postpartum. For admissions where MG was recorded as "any diagnosis" (primary or secondary), all admissions with MG were included in the time categories prepregnancy and postpartum. In the time category "pregnancy," we chose to only include admissions which had the primary diagnosis codes for MG or ICD-10 codes O993 (diseases of the nervous system complicating pregnancy), O998 (other specified diseases complicating pregnancy), and ICD-9 codes starting with 646 (other complications of pregnancy not elsewhere classified). This was to avoid counting all purely pregnancy-related admissions during pregnancy as MG-related admissions. None of the women were admitted during pregnancy for causes unrelated to MG or pregnancy. Hospitalizations for MG onset were not counted as events.

Women were followed from MG onset (or from January 1, 1987, if earlier) until December 31, 2019, or death. Two women with MG onset during pregnancy are described separately in the Results section. Owing to within-individual comparisons, it was only deemed necessary to adjust for 2 time-dependent confounders: thymectomy within the past year and disease duration less than 2 years because short disease duration is known to increase the risk of MG exacerbation and the beneficial effect of thymectomy can take at least 1 year. Age was adjusted for by using attained age as the time scale. Robust standard errors (the Huber sandwich estimator) were used to handle the dependency that arose from recurrent events and multiple pregnancies per woman. Postpartum periods that overlap with a subsequent pregnancy were terminated at the start of the subsequent pregnancy and prepartum periods for the subsequent pregnancy were shortened.

To assess whether women may be more likely to conceive during periods of relative disease stability, an additional analysis was performed using 4 time categories: prepregnancy, pregnancy, postpartum, and outside pregnancy. Outside pregnancy was defined as any period where the woman appears in the registers from 1987 to 2019 which is not 1 year before pregnancy, during pregnancy, and up to 1 year after pregnancy. All statistical analyses were performed using R version 4.4.2 by an experienced biostatistician (K.G.).

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Swedish Ethical Review Authority (Dnr: 2025-03787-02, 2024-04074-02, and 2023-05123-02). As this was a nationwide register-based study, the requirement for individual informed consent was waived. The data sets provided to the researchers from the registers were pseudonymized using unique serial numbers before analysis.

Data Availability

All data supporting the findings of this study are included in the article and its Supplementary Information. Owing to GDPR regulations, individual-level data cannot be shared publicly but may be made available upon reasonable request under a data-sharing agreement that ensures participant confidentiality.

Results

Cohort Characteristics

The study population consisted of 112 women with MG with 176 singleton pregnancies (Table 1). The median maternal age at the time of pregnancy was 30 years, and the median duration of MG at that time was 8 years (IQR 3.6–12.8 years). Approximately half (46%) of the pregnancies represented the woman's first pregnancy that reached week 22 + 0, and the majority (72%) occurred after the year 2000. Most women (88%) received care at a tertiary hospital. In terms of MG subgroups, most women had early-onset MG with AChR antibody seropositivity and thymus hyperplasia (Table 1). Three women had MuSK antibody seropositive MG, 1 had congenital MG diagnosed at 1 month of age, and 1 had juvenile-onset MG diagnosed age 12. A subset of women had seronegative MG. The most common MGFA class closest to pregnancy was MGFA class IIa, observed in 69 pregnancies (51.9%; Table 1), MGFA class was measured during or within a year of pregnancy in only 53% of pregnancies.

Primary Outcome Measure: Hospital Admissions With MG During Pregnancy and Postpartum

A total of 112 women with 176 pregnancies were included in the analysis (Table 2). The rate of hospital admissions with MG as the primary diagnosis did not differ significantly between pregnancy and the year preceding pregnancy (HR 0.74, 95% CI 0.39–1.41), and the risk of prolonged hospital admissions (measured as nights in hospital) was not elevated during pregnancy (HR 0.83, 95% CI 0.36–1.88). Similarly, admission rates were not significantly higher in the first year postpartum (HR 1.44, 95% CI 0.55–3.75, Table 2). However,

Table 1 Maternal Baseline Characteristics (n = 176 Pregnancies in 112 Women)

Characteristic		
Age (y) (median [IQR])	30.0 (27.0–34.0)	
Disease duration (y) [median (IQR)]	8 (3.6–12.8)	
MGFA class (missing data 25.9%), n (%)	Closest to pregnancy[a] (pregnancies)	Worst ever MGFA class (women)
Asymptomatic	23 (17.3)	4 (4.1)
MGFA class I	6 (4.5)	5 (5.1)
MGFA class IIa	69 (51.9)	37 (37.8)
MGFA class IIb	19 (14.3)	16 (16.3)
MGFA class IIIa	11 (8.3)	14 (14.3)
MGFA class IIIb	2 (1.5)	10 (10.2)
MGFA class IVa	2 (1.5)	6 (6.1)
MGFA class IVb	0 (0)	1 (1.0)
MGFA class V	0 (0)	5 (5.1)[b]
Thymectomy before delivery, n (%)	130 (73.9)	
Antibodies (missing data 18.7%), n (%)		
AChR ab seropositive	73 (80.2)	
MuSK ab seropositive	3 (3.3)	
Titin ab	1 (1.1)[c]	
AChR ab seronegative	7 (7.7)	
AChR/MuSK ab seronegative	6 (6.6)	
AChR/MuSK/Lrp4 ab seronegative	2 (2.3)	
Thymus histology (missing data 45.4%), n (%)		
Hyperplasia	51 (83.6)	
Normal/atrophy	5 (8.2)	
Thymoma	5 (8.2)	
Neurophysiology (missing data 54.5%), n (%)		
Abnormal RNS	38 (76.0)	
Abnormal SFEMG	8 (16.0)	
Normal RNS, SFEMG not tested	2 (4.0)	
Normal RNS + SFEMG	2 (4.0)	
MG medications ever treated with (missing data 5.6%), n (%)		
AChEI	91 (85.5)	
Corticosteroids	47 (43.9)	
Azathioprine	21 (19.9)	
IVIG/plasmapheresis	20 (18.7)	
Rituximab	20 (18.6)	
Cyclosporine	11 (10.8)	
Mycophenolate mofetil	3 (3.0)	

Continued

Table 1 Maternal Baseline Characteristics (n = 176 Pregnancies in 112 Women) *(continued)*

Characteristic	
Country of birth, n (%)	
Sweden	87 (77.7)
Europe other	14 (12.5)
Non-European	12 (10.7)
Treating Hospital, n (%)	
Tertiary	99 (88.4)
Regional	13 (11.6)
Parity, n (%)	
1	81 (46.0)
2	70 (39.8)
3	19 (10.8)
4	5 (2.8)
5	1 (0.6)
Year of delivery, n (%)	
1987–1990	8 (4.5)
1991–2000	41 (23.3)
2001–2010	48 (27.2)
2011–2020	79 (45.0)

Abbreviations: AChR ab = Acetylcholine receptor antibody; MuSK = Muscle-specific tyrosine kinase antibody; LRP = ab low-density lipoprotein-related protein antibody; RNS = repetitive nerve stimulation; SFEMG = single-fiber electromyography.
[a] MGFA class "closest to pregnancy" was assessed during or within 1 year of pregnancy in 53% of pregnancies.
[b] Among these women, 2 were confirmed to have been intubated in intensive care and 3 were most likely intubated.
[c] This woman tested seropositive for both AChR and titin antibodies. Parity refers to the number of births (live or stillbirths ≥22 weeks of gestation).

the duration of hospital admissions was significantly increased during the postpartum year (HR 4.52, 95% CI 1.26–16.14, Table 2, Figure 1A). A comparable pattern was observed when MG was recorded as any diagnosis (primary or secondary; Table 2).

Cox regression analysis, designed to assess whether women are more likely to conceive when their MG is unusually stable, compared hospital admissions across 4 time frames: prepregnancy, pregnancy, postpartum, and nonpregnancy periods. The risk of prolonged hospital stays for MG was higher outside of pregnancy compared with the prepregnancy year (HR 2.73, 95% CI 1.13–6.56 for MG as any diagnosis; HR 2.95, 95% CI 0.84–10.43 for MG as primary diagnosis; Figure 1B).

When restricting to the "classic" postpartum period (the first 3 months after delivery), the risk of prolonged hospital stays remained elevated (Table 2, Figure 1C). For MG as the primary diagnosis, the HR was 5.02 (95% CI 1.66–15.24), and for MG as any diagnosis, the HR was 4.88 (95% CI 1.95–12.22) (Table 2, Figure 1D). Sensitivity analyses excluding 1 outlier with a hospital stay exceeding 100 days yielded consistent results (HR 3.26, 95% CI 1.08–9.84 for MG as primary diagnosis; HR 3.52, 95% CI 1.45–8.56 for MG as any diagnosis).

The timing and duration of MG-related hospitalizations across all periods are illustrated in Figures 2 and 3.

Characteristics of Women Hospitalized Postpartum

In total, 19 pregnancies (10.8%) in 16 women required at least 1 hospital admission for MG as the primary diagnosis in the first year postpartum, compared with 12 pregnancies (6.8%) in 11 women in the year before pregnancy. Among the 16 women with postpartum admissions, 9 (56%) had at least 1 additional pregnancy after MG diagnosis without requiring hospitalization, indicating that postpartum exacerbations were not always consistent across pregnancies in the same individual (Table 3).

MG Onset During Pregnancy

Two women developed MG during pregnancy and were therefore not included in the main Cox regression analysis. Both presented with ocular symptoms and required brief inpatient care. Deliveries were uncomplicated. One patient was AChR antibody seronegative with abnormal single-fiber EMG

Table 2 Cox Regression Analysis: Rate and Duration of Hospital Admissions for MG During Pregnancy and Up to 1 Year Postpartum Compared With the Year Before Pregnancy (n = 176 Pregnancies in 112 Women)

Analysis (time)	Outcome	During pregnancy HR (95% CI)	Postpartum HR (95% CI)
Up to 3 mo postpartum	Hospital admissions		
	MG primary diagnosis	0.74 (0.41–1.34)	1.71 (0.65–4.47)
	MG any diagnosis	0.77 (0.48–1.25)	1.73 (0.79–3.79)
	Nights in hospital		
	MG primary diagnosis	0.75 (0.32–1.75)	5.02 (1.66–15.24)[b]
	MG any diagnosis	0.73 (0.36–1.48)	4.88 (1.95–12.22)[b]
Up to 1 y postpartum	Hospital admissions		
	MG primary diagnosis	0.74 (0.39–1.41)	1.44 (0.55–3.75)
	MG any diagnosis	0.82 (0.49–1.35)	1.39 (0.63–3.07)
	Nights in hospital		
	MG primary diagnosis	0.83 (0.36–1.88)	4.52 (1.26–16.14)[b]
	MG any diagnosis	0.82 (0.42–1.60)	3.93 (1.32–11.70)[b]
Sensitivity[a] – 3 mo postpartum	Nights in hospital		
	MG primary diagnosis	0.60 (0.25–1.41)	3.26 (1.08–9.84)[b]
	MG any diagnosis	0.62 (0.30–1.25)	3.52 (1.45–8.56)[b]

The period before pregnancy serves as the reference period. The model is adjusted for time-dependent covariates: MG onset within 2 years and thymectomy within 1 year.
[a] Sensitivity analysis performed after excluding 1 woman with unusually prolonged hospital admissions.
[b] p = <0.05.

during pregnancy; the other was MuSK antibody seropositive. Postpartum, one underwent thymectomy without further exacerbations and the other experienced a relapse requiring immunotherapy. The maximum MGFA class observed was II.

Secondary Outcome Measure: Changes in MG Medications Around Pregnancy

Changes in symptomatic and immunosuppressive MG medications are reported during and after pregnancy in Figure 4. One hundred sixty-three of the 176 pregnancies in the study were recorded in the medication registers. In 13 pregnancies, immunosuppressive MG medications were successfully reduced during pregnancy without the need for switching to alternative agents. In an additional 4 pregnancies, AChEIs were discontinued, with "stable MG" noted as the reason in the MG register. Conversely, immunosuppressives were initiated during pregnancy in 6 pregnancies.

In the year after delivery, immunosuppressive medications were initiated or escalated in 10 pregnancies. In contrast, no cases of reduction or discontinuation of immunosuppressive treatment were recorded, except for 1 case in which AChEI therapy was stopped postpartum.

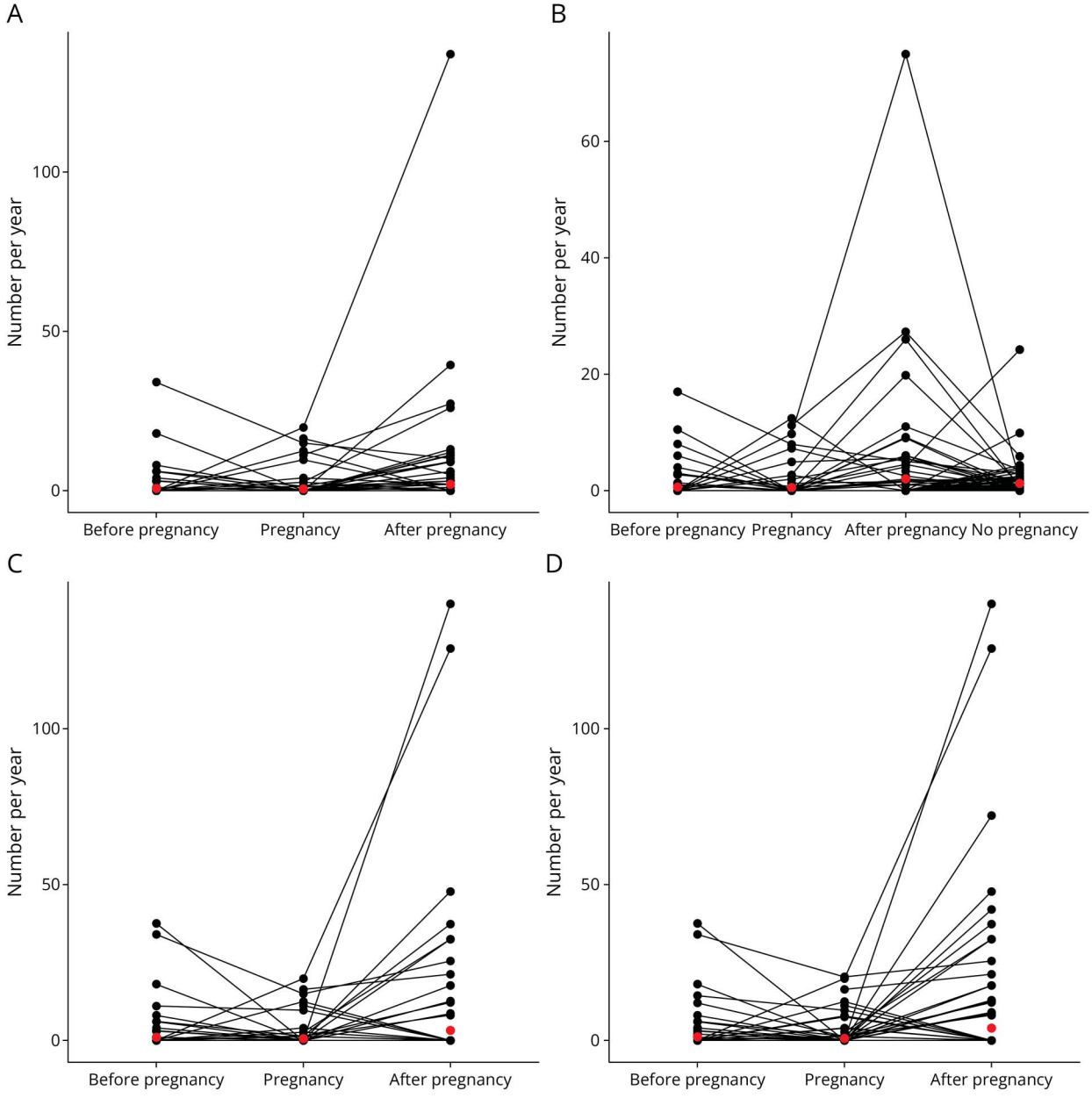
The timing of introduction or escalation of immunosuppression postpartum varied: corticosteroids were introduced at 5 days, 3 months, 5 months, and 9 months after delivery; azathioprine at 1 month and twice at 3 months; IVIG at 2 weeks and 2 months; and tacrolimus at 10 months postpartum. In total, escalated MG treatment was needed during or after pregnancy in 16 pregnancies. In 6 women who required treatment escalation in at least one 1 pregnancy, other pregnancies in the same woman showed no such need. In 1 case, immunosuppression was even reduced in a subsequent pregnancy.

Discussion

In this nationwide cohort study, we found no evidence of an increased risk of MG exacerbation during pregnancy, as measured by the rate or duration of MG-related hospital admissions. Women were more likely to conceive during periods of relative clinical stability, and nearly 90% had no MG-related hospital admissions in the first year postpartum. However, a subset of women experienced exacerbations in the first year postpartum, with a significantly higher risk of prolonged MG-related hospital admissions, reflecting more severe or prolonged exacerbations.

Changes in immunosuppressive therapy around pregnancy supported the observed clinical stability during pregnancy.

Figure 1 Spaghetti Plots Illustrating the Number of Hospital Nights per Year per Woman With Myasthenia Gravis (MG) in Relation to Pregnancy

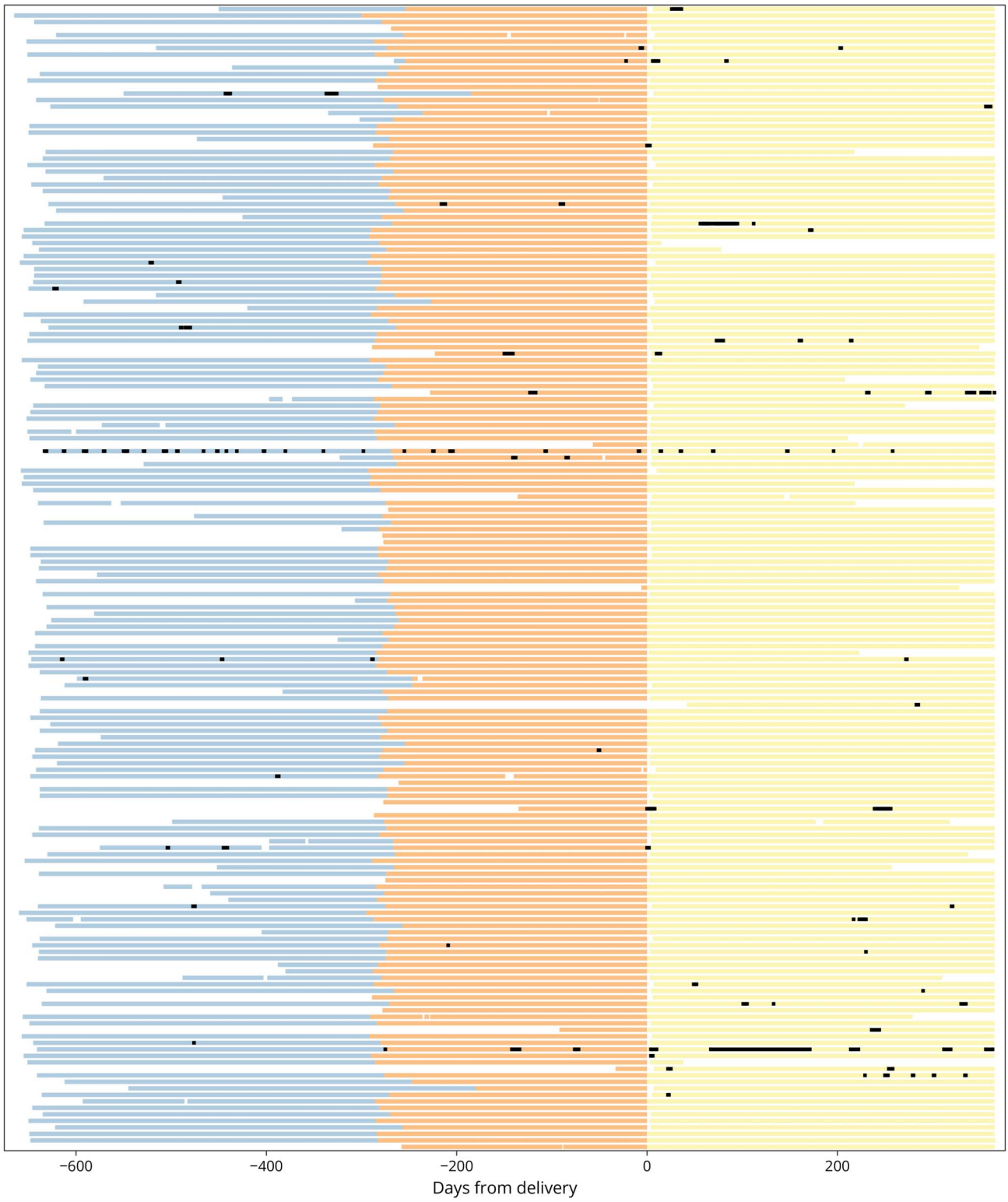


Panels A–C show hospital nights where MG was recorded as the primary diagnosis: (A) 1 year before pregnancy, during pregnancy, and up to 1 year postpartum; (B) the same periods as in A, plus additional periods outside pregnancy 'no pregnancy'; (C) when the postpartum period is defined as 3 months. Panel D shows hospital nights for MG as any diagnosis (primary or secondary) 1 year before pregnancy, during pregnancy, and up to 3 months postpartum. Red points indicate mean values for each period.

While some treatment reductions may have reflected concerns regarding fetal exposure to immunosuppressants, the overall pattern suggests that disease control was generally maintained. By contrast, treatment initiation or intensification was more frequent postpartum, with no recorded cases of treatment reduction, suggesting a higher likelihood of exacerbations after delivery in a subset of women.

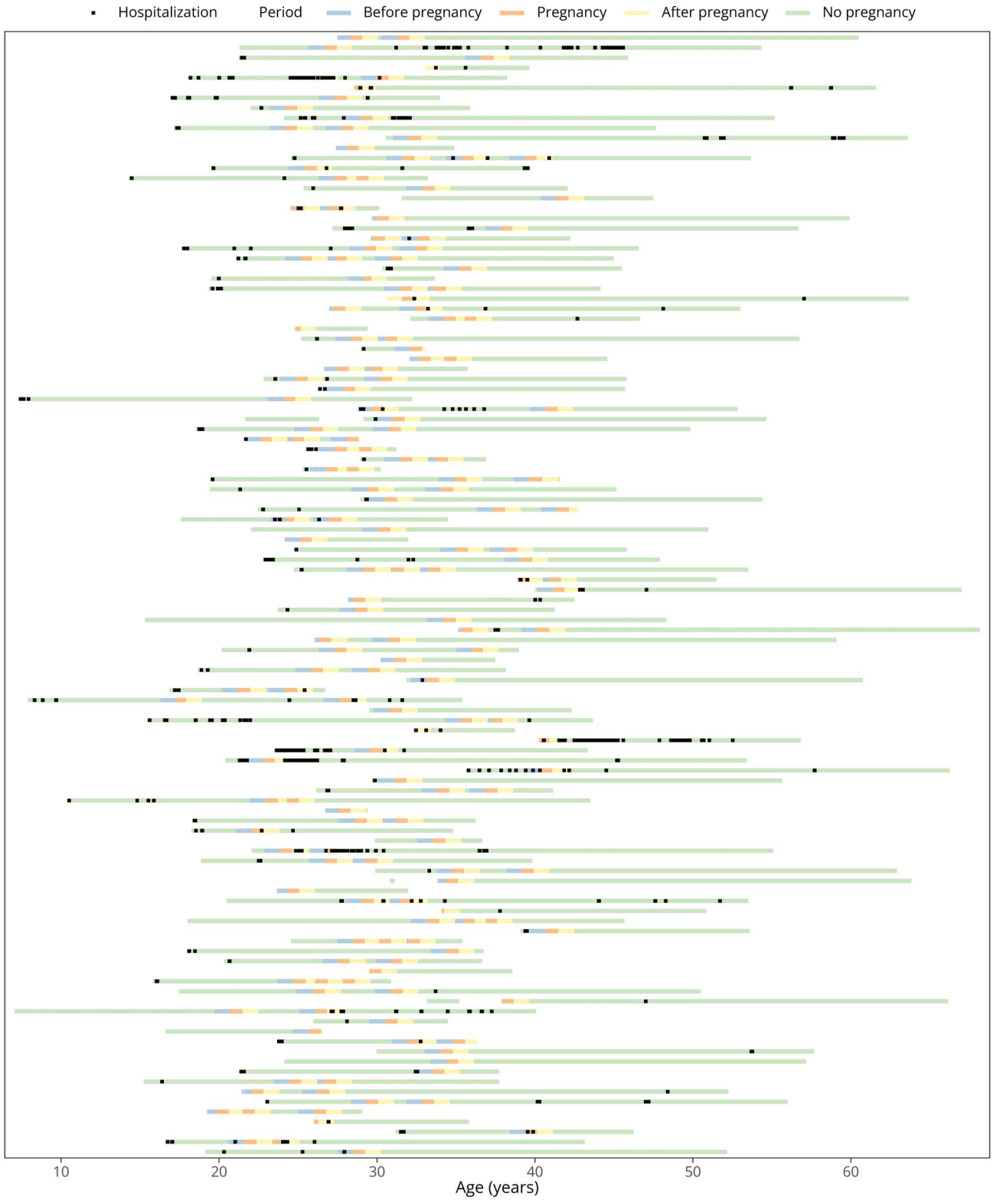
Among the 16 women who required postpartum hospitalization for MG, just over half had at least one other pregnancy in which no postpartum hospitalization occurred. Similarly, escalation of immunosuppressive therapy was not consistently required across pregnancies in the same woman. This intraindividual variability underscores the complexity of MG disease course in relation to pregnancy and highlights the challenge of predicting exacerbations based on prior pregnancy outcomes. The absence of reliable biomarkers for MG exacerbations outside of pregnancy, combined with hormonal, immunologic, and disease-specific dynamics surrounding pregnancy, further complicates risk stratification.

Figure 2 Timing and Duration of Hospital Admissions With Myasthenia Gravis (MG) as the Primary Diagnosis During the Periods 1 Year Before, During Pregnancy, and Up to 1 Year Postpartum



A previous study has showed a clear increased risk for MG disease onset postpartum.[10] Previous studies on risk of exacerbation in established disease have yielded mixed results, with some reporting a modest increase in exacerbation postpartum, in alignment with our findings, and others finding no clear association.[7,8,11-14] A meta-analysis estimated that

Figure 3 Timing and Duration of Hospital Admissions With Myasthenia Gravis (MG) as the Primary Diagnosis Across the Entire Longitudinal Follow-Up Period in the National Registers, Including Periods Around Pregnancy and Periods Not Around Pregnancy



among MG exacerbations around pregnancy, 11% occurred postpartum, compared with 23% during pregnancy.[8] Our population-based data indicate that postpartum exacerbations, although infrequent, can be more severe or prolonged when they do occur. This pattern of postpartum vulnerability mirrors other autoimmune diseases, such as multiple sclerosis and

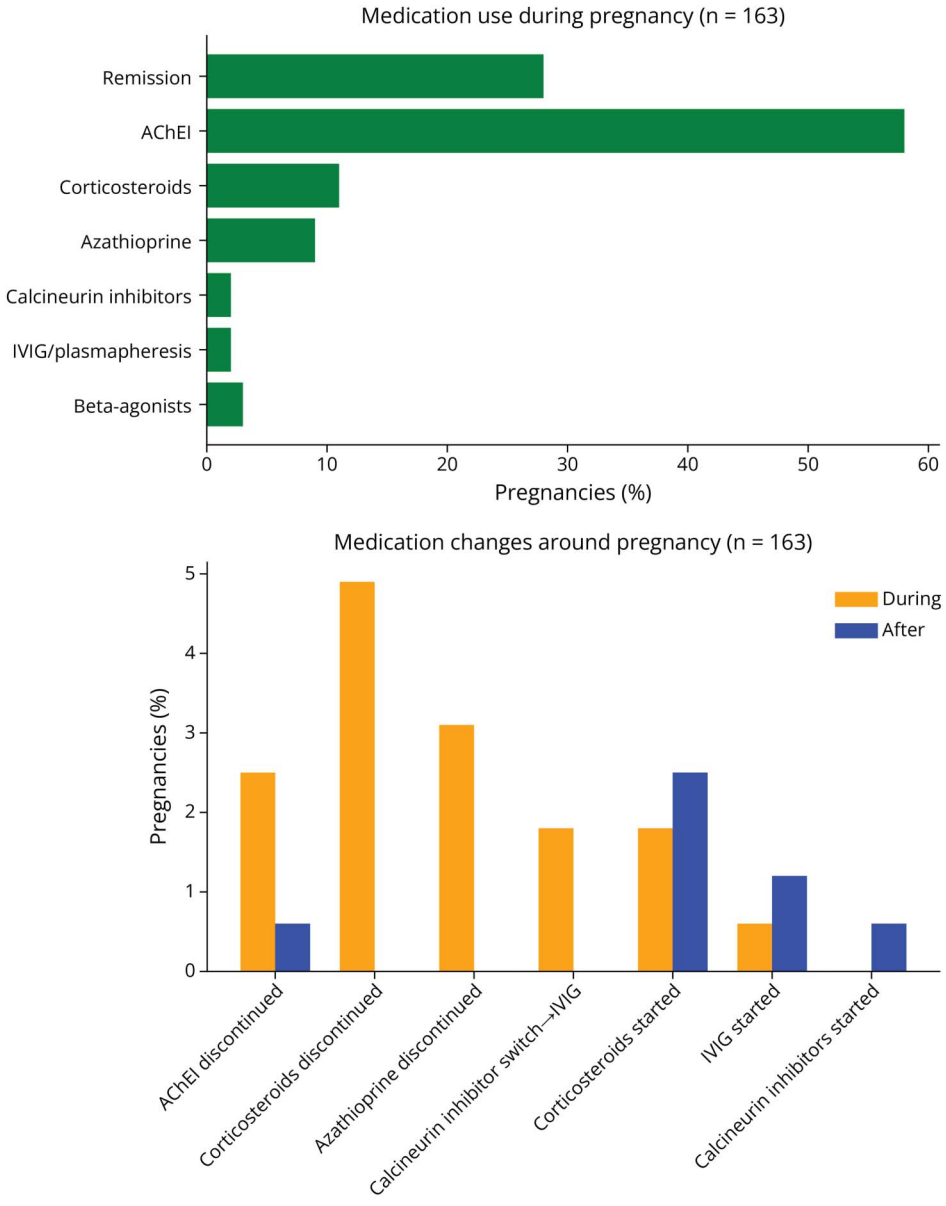
Table 3 Characteristics of Women Hospitalized With MG as the Primary Diagnosis Up to 1 Year Postpartum (n = 16 Women With 19 Pregnancies)

Characteristics	n (%)	
Duration of postpartum stay (nights), (%)		
≤3 nights	8 (42)	
4–7 nights	2 (11)	
8–21 nights	8 (37)	
>21 nights	2 (11)	
Parity, (%)		
1	7 (37)	
2	11 (58)	
3	0 (0)	
4	1 (5)	
MGFA class	Closest to pregnancy,[a] (%)	Worst ever, (%)
IIa	13 (68)	10 (53)
IIb	1 (5)	1 (5)
IIIa	1 (5)	3 (16)
IIIb	1 (5)	2 (10)
Iva	1 (5)	1 (5)
Missing data	2 (10)	2 (10)
Disease duration (y)		
Median (IQR)	9 (6.5–17.5)	
Antibodies, (%)		
AChR ab	9 (56)	
MuSK ab	1 (6)	
AChR/MuSK ab seronegative	4 (25)	
Missing data	2 (13)	
Thymectomy before pregnancy	14 (88)	
Medications during pregnancy, (%)		
AChEI	9 (47)	
AChEI + Azathioprine	4 (21)	
AChEI + Cyclosporine	1 (5)	
Azathioprine	1 (5)	
Cyclosporine	1 (5)	
None documented	2 (10)	

Abbreviations: AChR ab = acetylcholine receptor antibody; AChEI = acetylcholinesterase inhibitors; MuSK ab = muscle-specific tyrosine kinase antibody.
[a] MGFA class was often not documented within 1 year of pregnancy.

rheumatoid arthritis, which often improve during pregnancy but worsen after delivery.[15,16] Immunologic and hormonal shifts following childbirth, combined with physical stressors such as sleep deprivation and fatigue, may contribute to exacerbations in a subset of women with MG. Recent biomarker studies support this hypothesis, showing declines in anti-inflammatory plasma proteins during the postpartum transition, reflecting altered immune regulation.[17]

Figure 4 Use of Symptomatic and Immunosuppressive Medications for Myasthenia Gravis (MG) During Pregnancy and Changes in Medication Use During Pregnancy and Up to 1 Year Postpartum



AChEI = acetylcholinesterase inhibitors; IVIg = IV immunoglobulins.

A major strength of this study is its large, population-based design, making it, to our knowledge, the largest cohort study to date examining MG disease course during and after pregnancy. By linking multiple nationwide registers, we captured longitudinal data spanning 3 decades, including hospital admissions, medication use, and clinical characteristics. This comprehensive approach enabled within-individual comparisons and minimized recall bias, providing a robust understanding of MG exacerbation trajectories in relation to pregnancy.

Limitations include incomplete coverage of the voluntary MG register. Clinical severity scores were incomplete, particularly before 2001, limiting the standardized definitions of exacerbation. Therefore, the Inpatient Register, which records all hospital admissions from 1987, was used to capture the outcome of MG exacerbations requiring hospital admission. Reliance on hospital admissions as a proxy for MG exacerbations risks capturing only the more severe exacerbations. Exacerbations were also captured by examining changes in MG medications, however medication data were incomplete, and dose adjustments may have gone undocumented. A validation study showed high agreement for chronic medications but low for occasional use and systemic corticosteroids.[18] We did not adjust for temporal changes in MG treatment, as individual-level effects were likely minimal, and our study concluded in 2019 before complement inhibitors and neonatal Fc receptor inhibitors were introduced in Sweden. Our

findings apply only to pregnancies reaching ≥22 + 0 weeks, and breastfeeding data were unavailable. The predominance of tertiary care settings may limit generalizability to broader MG populations. Nonetheless, consistency across complementary outcome measures strengthens the validity of our findings. Future prospective, international studies with detailed baseline phenotyping and longitudinal follow-up are warranted to better capture exacerbation severity and the impact of newer MG therapies on maternal outcomes.

In this nationwide cohort study, pregnancy was not associated with an increased risk of MG exacerbation, providing reassurance for women planning pregnancy. The postpartum period carried a modest but clear risk of severe or prolonged exacerbations in a minority of women. Exacerbations varied across pregnancies within the same individual, highlighting the unpredictability of MG in the peripartum period. Vigilant postpartum monitoring and individualized care remain essential.

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Author Contributions

L. O´Connor: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. K. Gabrysch: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. A.-K. Wikström: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. A. Rostedt Punga: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data.

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