

Pregnancy in Generalized Myasthenia Gravis: A Real-World Study of Clinical and Economic Outcomes

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Abstract

Background

Knowledge of clinical and economic outcomes of generalized myasthenia gravis (gMG) in pregnancy remains limited.

Methods

A retrospective observational study used United States (U.S.) administrative claims from Komodo Research Database (01/2016–9/2023) to identify women aged 18–49 years with pregnancy (index date) with and without gMG and without pregnancy (random index date) with gMG. Follow-up period spanned index date to six months postpartum in pregnant cohorts. The reference cohorts (pregnant without MG and non-pregnant with gMG) were matched 10:1 to the pregnant with gMG cohort on the duration of the follow-up period. Cohorts were balanced using entropy weighting. Outcomes were analyzed using weighted regressions.

Results

97 pregnant women with gMG, 970 pregnant women without MG, and 970 non-pregnant women with gMG were included. Pregnant women with gMG had 2.50 times higher odds of preterm birth and 2.64 times higher odds of Cesarean section vs. those without MG; had 3.90 times higher odds of MG crisis and fewer monthly days with treatment supply (mean differences: -4.0 days for immunosuppressants; -1.5 for rituximab; -1.1 for complement C5 inhibitors) vs. non-pregnant women with gMG (all $p < 0.05$). Among pregnant women, those with gMG had \$3,170 higher mean monthly total healthcare costs vs. those without MG; among women with gMG, those with pregnancy had \$3,483 lower gMG pharmacy costs vs. those without (all $p < 0.05$).

Conclusions

Pregnant women with gMG faced higher risks of adverse pregnancy outcomes and MG crisis while receiving fewer MG-related treatments, highlighting the need for proactive management and further research.

BACKGROUND

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by the production of autoantibodies that target components at the neuromuscular junction, leading to impaired communication between nerves and muscles [1]. The hallmark symptom of MG is fatigable muscle weakness [1, 2]. In approximately 15% of individuals, symptoms are limited to the ocular muscles [3]. The remaining majority have generalized MG (gMG), which involves muscle groups including those responsible

for swallowing, chewing, speech, respiration, and limb movement [4]. In 2021, the estimated prevalence of MG in the United States (U.S.) was 37 per 100,000 individuals [5], with women under 40 years of age being particularly affected [1]. As gMG commonly occurs during the reproductive years, it is essential to understand how pregnancy influences disease progression and treatment options, as well as how MG may impact maternal and fetal outcomes.

Pregnancy and gMG can influence each other in clinically important ways [6]. Disease exacerbations can occur at any point during pregnancy, with some studies suggesting a higher risk during the first trimester and postpartum periods [7–9]. A prior systematic review reported an overall exacerbation rate of about 34% during pregnancy, with myasthenic crises occurring in 6% of patients during pregnancy and 8% postpartum [10]. Additionally, data from a U.S. national inpatient sample showed that pregnant women with gMG had higher rates of respiratory failure, preterm delivery, low birthweight, feeding problems, and longer hospital stays compared to those without MG [10–12]. Despite these insights, there remains a lack of comprehensive U.S.-based studies describing both MG-related clinical events and pregnancy outcomes in women with gMG.

Current treatment guidelines provide tailored recommendations for managing gMG in women who are pregnant or may become pregnant, often with more limited therapeutic options compared to the general population [6, 13]. For pregnant women, oral pyridostigmine (an acetylcholinesterase [AChE] inhibitor) is the preferred first-line therapy, while intravenous AChE inhibitors are generally avoided due to the risk of uterine contractions [13]. Corticosteroids (i.e., prednisone and prednisolone) are also considered safe therapeutic options during pregnancy [14]. Several immunosuppressants are contraindicated during pregnancy due to potential teratogenic effects [13, 15]. Rituximab, a monoclonal antibody, leads to transient B-cell depletion in newborns [16]. Thymectomy, although effective for some individuals, is typically deferred during pregnancy due to surgical risks and limited benefit during this period [4, 13, 17, 18]. Acute treatments such as plasma exchange and immunoglobulin are used for managing myasthenic crises and can be considered during pregnancy with careful risk-benefit assessment [13]. More recently, the development of targeted immunotherapies, including complement C5 inhibitors (C5i) and neonatal Fc receptor (FcRn) blockers, have broadened treatment options [19–22]. While data on their use in pregnancy remain limited, emerging studies suggest some of these agents may have acceptable safety profiles for both mother and fetus [23, 24].

To address the current evidence gap and inform clinical decision-making, this study's objectives were to evaluate pregnancy outcomes, rates of MG exacerbation and crisis, gMG-related treatment use, healthcare resource utilization (HRU) and healthcare costs among pregnant women with gMG in a large U.S. population using comprehensive longitudinal data. These outcomes were compared between pregnant women without MG and non-pregnant women with gMG.

METHODS

Data source

This study used U.S. administrative claims data from Komodo Research Data (KRD+), covering January 1, 2016 through September 30, 2023. KRD+ comprises pharmacy and inpatient and outpatient medical claims sourced from over 150 payers and includes records for more than 160 million individuals across all U.S. regions. To ensure a socioeconomically diverse sample, KRD+ draws from commercial insurance, Medicare Advantage, and Medicaid.

Available claims data include service dates, diagnostic and procedure codes, provider types, medication dispensed, and estimated allowed amounts for costs [25]. Additionally, the dataset provides health insurance eligibility and key demographic information, such as sex, year of birth, and race/ethnicity. KRD+ data are de-identified in accordance with the Health Insurance Portability and Accountability Act regulations.

Study design

A retrospective observational study design was employed to examine the cohort of pregnant women with gMG (*pregnant with gMG cohort*) against two comparator cohorts, independently: (i) pregnant women without MG (*pregnant without MG cohort*), and (ii) non-pregnant women with gMG (*non-pregnant with gMG cohort*). The study period extended from January 1, 2016 through March 30, 2023, concluding six months before the end of data.

For the two pregnant cohorts (i.e., with gMG and without MG), the index date was the estimated date of the last menstrual period of their first observed pregnancy, using a validated claims-based algorithm [26]. For the non-pregnant with gMG cohort, the index date was a randomly assigned date during the intake period.

The 12-month period preceding the index date was defined as the baseline period. The follow-up period in the two pregnant cohorts spanned from the index date to the 6-month postpartum period, which started from any of the following: the delivery date for live births, the date of abortion/miscarriage, the date of ectopic pregnancy removal, or the date of stillbirth. The pregnant without MG cohort and the non-pregnant with gMG cohort were matched 10:1 to the pregnant with gMG cohort on the duration of the follow-up period and the quarter and year of index date to remove the influence of differential follow-up duration on the ability to observe study outcomes and to account for any secular trends.

Study samples

Women in the pregnant cohorts were required to have evidence of pregnancy during the study period, based on an identification algorithm developed by Sarayani et al. [26]. This algorithm was based on a previously validated algorithm (Matcho et al. [27]) developed for the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes, and further adapted for use with the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnostic codes. Women in the non-pregnant cohort had no evidence of pregnancy during the study period.

Women in the gMG cohorts were required to have evidence of gMG during the baseline period. The criteria to identify gMG were adapted from Phillips G et al. [28] and Zhdanova et al. [29, 30], and included the following: (i) ≥ 1 claim with a principal diagnosis for MG (ICD-10-CM: G70.00 or G70.01) in an inpatient setting or ≥ 2 claims on separate days ≥ 1 month apart in an outpatient, emergency room (ER), or other setting during the baseline period or on the index date; (ii) ≥ 1 claim with a diagnosis of MG made by a neurologist during the baseline period or on the index date; (iii) no claims with diagnoses for congenital MG (ICD-10-CM: G70.2) during the baseline period or on the index date. Women in the pregnant without MG cohort had no evidence of MG during the study period.

All cohorts included only women aged 18–49 years old on the index date and continuously eligible for health insurance ≥ 12 months before and ≥ 6 months after the index date.

Study outcomes

Pregnancy outcomes included delivery of live births, spontaneous or induced abortions, termination of ectopic pregnancies, and stillbirths (defined based on the validated claims-based algorithm) [26]. Among those with live births; gestational age, preterm births, and the use of Cesarean sections were also reported based on diagnostic and procedures codes. Preterm births were defined as a live birth before 37 weeks of gestation. Extreme preterm (< 28 weeks), very preterm (28–31 weeks) and moderate-to-late preterm (32–37 weeks) were also reported.

MG exacerbations were identified in medical claims using any of the following: (i) a diagnostic code for MG with exacerbation (ICD-10-CM: G70.01) in any position or setting, or (ii) a diagnosis code for MG without exacerbation (G70.00) in any position or setting accompanied on the same day or during the same inpatient admission by a diagnostic code of dyspnea, respiratory failure, disease of the diaphragm, or (iii) a diagnostic code for MG without exacerbation (G70.00) in any position in an inpatient setting accompanied by a diagnostic code of dysphagia or intravenous immunoglobulin use.

MG crisis was defined in medical claims as a procedure for intubation, tracheostomy or mechanical ventilation with a diagnosis of MG in the same inpatient or intensive care unit admission.

Use of gMG-related medications (**Supplementary Table S1**) was measured monthly of days with supply to capture the intermittent nature of medication use [31]. Days of supply were obtained directly from pharmacy claims and imputed for medical claims using the mode of days of supply on the class level observed in pharmacy claims. For the pregnant with gMG cohort, the proportion of those who received treatments contraindicated in pregnancy were summarized by trimester (first trimester: conception to 13 weeks 6 days; second-to-third trimester: 14 weeks to the pregnancy end date), the postpartum period (day after pregnancy end date to 6 months), and the entire follow-up period (pregnancy start to 6 months postpartum).

HRU and healthcare costs were assessed monthly using both pharmacy and medical claims. Healthcare costs corresponded to the estimated total payment, representing the sum of payer's reimbursed amount

and individual's out-of-pocket expense for a service and were adjusted for inflation using the U.S. Consumer Price Index and reported in 2023 U.S. dollars.

gMG-related medical costs were identified from medical claims with an ICD-10-CM diagnostic code for MG (i.e., G70.0, G70.01). Pregnancy-related medical costs were based on medical claims with an ICD-10-CM diagnostic code indicating evidence of pregnancy (**Supplementary Table S2**).

In the comparison of the pregnant with gMG cohort to the non-pregnant with gMG cohort, only gMG-related HRU and costs were reported, as differences in all-cause costs would mainly reflect pregnancy-related costs and would not be relevant to the objectives of this study.

Statistical analyses

To adjust for differences in baseline characteristics, the control cohorts (i.e., pregnant without MG cohort and non-pregnant with gMG cohort) were re-weighted against the pregnant with gMG cohort using entropy balancing [32]. The following baseline characteristics were used to re-weight: age, race, geographic region, payer, index quarter, and the Quan-Charlson Comorbidity Index [33]. In addition, the pregnant with gMG cohort and the non-pregnant with gMG cohort were re-weighted on the presence of the common physical and psychiatric comorbidities to account for the fact that pregnancy is correlated with better state of health compared with the non-pregnant state. Balance of baseline characteristics after weighting was assessed using standardized differences (< 10% was considered well balanced) [34].

Outcomes were then compared between the weighted cohorts over the follow-up period using weighted regression models. Baseline comorbidities that remained unbalanced after weighting were included as covariates in the models. Logistic regression was applied to binary outcomes, with results reported as odds ratios (OR) with 95% confidence intervals (CI) and p-values. Count variables were compared as rate ratios using Poisson regression models and non-parametric bootstrap procedures with 500 Poisson regression replications were used to produce 95% CI and p-values. Continuous variables were compared as mean cost difference using ordinary least squares (OLS) regressions, and non-parametric bootstrap procedures with 500 OLS replications were used to produce 95% CI and p-values.

All analyses were conducted using SAS® Enterprise Guide® version 8.3, SAS Institute, Cary, NC, U.S., and R version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria.

RESULTS

Baseline characteristics

A total of 97 pregnant women with gMG, along with 970 pregnant women without MG and 970 non-pregnant women with gMG were included in the study (Table 1). Across all three cohorts, mean age was 32 years; 38% were White, 13% were Black or African American, 20% were of another race or ethnicity, and the remaining 29% had unknown race/ethnicity. Among the pregnant with gMG cohort, the most common

physical comorbidities noted during the baseline period were obesity (25.8%), neurological condition other than gMG (20.6%), and deficiency anemias (16.5%); the most common psychiatric comorbidities were anxiety disorders (35.1%), depressive disorders (16.5%), and sleep-wake disorders (13.4%). The baseline monthly all-cause healthcare costs were \$6,117 among the pregnant with gMG cohort, \$745 among the pregnant without MG cohort, and \$7,057 among the non-pregnant with gMG cohort.

Table 1
Baseline characteristics^a

Mean ± SD [median] or n (%)	Pregnant with gMG	Non- pregnant with gMG	Std. diff.	Pregnant without MG	Std. diff.
	N = 97	N = 970	%	N = 970	%
Age at index date (years)	32.2 ± 6.0 [33.0]	32.3 ± 6.5 [33.1]	1.9	32.3 ± 5.9 [33.1]	1.3
Race/ethnicity					
White	37 (38.1)	370 (38.2)	0.0	370 (38.1)	0.0
Hispanic or Latino, Asian or Pacific Islander, or Other	19 (19.6)	190 (19.6)	0.0	190 (19.6)	0.0
Black or African American	13 (13.4)	130 (13.4)	0.0	130 (13.4)	0.0
Unknown	28 (28.9)	280 (28.9)	0.0	280 (28.9)	0.0
Geographic region					
South	37 (38.1)	370 (38.1)	0.0	370 (38.1)	0.0
Northeast	28 (28.9)	280 (28.9)	0.0	280 (28.9)	0.0
Midwest	18 (18.6)	180 (18.6)	0.0	180 (18.6)	0.0
West	14 (14.4)	140 (14.4)	0.0	140 (14.4)	0.0
Unknown	0 (0.0)	0 (0.0)	0.0	0 (0.0)	0.0
Payer^b					
Commercial	70 (72.2)	700 (72.2)	0.0	700 (72.2)	0.0
Medicaid	19 (19.6)	190 (19.6)	0.1	190 (19.6)	0.0
Medicare Advantage	8 (8.2)	80 (8.3)	0.1	80 (8.3)	0.1

Mean ± SD [median] or n (%)	Pregnant with gMG	Non- pregnant with gMG	Std. diff.	Pregnant without MG	Std. diff.
	N = 97	N = 970	%	N = 970	%
Common physical comorbidities					
Obesity	25 (25.8)	216 (22.3)	8.2	226 (23.3)	5.8
Hypertension	13 (13.4)	130 (13.4)	0.1	110 (11.4)	6.2
Hypothyroidism	15 (15.5)	150 (15.5)	0.1	154 (15.9)	1.1
Common DSM-5 conditions					
Anxiety disorders	34 (35.1)	340 (35.1)	0.0	250 (25.7)	20.4*
Depressive disorders	16 (16.5)	160 (16.5)	0.0	162 (16.7)	0.6
Sleep-wake disorders	13 (13.4)	130 (13.4)	0.0	63 (6.5)	23.1*
Other autoimmune disorder	17 (17.5)	170 (17.5)	0.0	86 (8.9)	25.7*
Weakness symptoms					
Dyspnea	22 (22.7)	229 (23.6)	2.3	141 (14.6)	44.1*
Malaise and fatigue	22 (22.7)	266 (27.5)	11.0*	0 (0.0)	20.9*
Diplopia	19 (19.6)	165 (17.0)	6.8	27 (2.8)	69.8*
General and other muscle-specific weakness	19 (19.6)	258 (26.6)	16.8*	10 (1.1)	55.5*
Dysphagia	18 (18.6)	109 (11.2)	20.7*	1 (0.1)	61.5*
Ptosis	18 (18.6)	128 (13.2)	14.7*	0 (0.0)	67.0*
Classes of therapy					

Mean ± SD [median] or n (%)	Pregnant with gMG	Non-pregnant with gMG	Std. diff.	Pregnant without MG		Std. diff.
	N = 97	N = 970	%	N = 970		%
AChE inhibitor	68 (70.1)	711 (73.3)	7.1	–		–
Systemic corticosteroid	54 (55.7)	589 (60.7)	10.3*	–		–
Non-steroidal immunosuppressant	23 (23.7)	372 (38.4)	32.1*	–		–
Immunoglobulin	20 (20.6)	224 (23.1)	6.0	–		–
Monoclonal antibody	6 (6.2)	55 (5.7)	2.2	–		–
Complement C5 inhibitor	2 (2.1)	32 (3.3)	7.7	–		–
Neonatal Fc receptor blocker	0 (0.0)	1 (0.1)	4.5	–	–	
≥ 1 MG exacerbation	37 (38.1)	411 (42.4)	8.6	–	–	
≥ 1 MG crisis	2 (2.1)	13 (1.3)	5.6	–	–	
Year of index date						
2017	20 (20.6)	183 (18.9)	4.4	200 (20.6)	0.0	
2018	17 (17.5)	149 (15.4)	5.8	170 (17.5)	0.0	
2019	17 (17.5)	189 (19.5)	5.1	170 (17.5)	0.0	
2020	20 (20.6)	196 (20.2)	1.1	200 (20.6)	0.0	
2021	13 (13.4)	148 (15.3)	5.4	130 (13.4)	0.0	
2022	9 (9.3)	100 (10.4)	3.6	90 (9.3)	0.0	
2023	1 (1.0)	5 (0.5)	6.4	10 (1.0)	0.0	
All-cause healthcare costs	6,117 ± 11,064 [1,214]	7,057 ± 14,871 [1,556]	7.2	745 ± 1,908 [198]	68.0*	

Mean $\pm$ SD [median] or n (%)	Pregnant with gMG	Non-pregnant with gMG	Std. diff.	Pregnant without MG	Std. diff.
	N = 97	N = 970	%	N = 970	%
All-cause pharmacy costs	3,528 $\pm$ 8,803 [203]	4,954 $\pm$ 13,677 [264]	12.4*	98 $\pm$ 356 [10]	55.3*
All-cause medical costs	2,589 $\pm$ 4,904 [799]	2,103 $\pm$ 4,529 [676]	10.3*	647 $\pm$ 1,816 [163]	52.8*

The mean duration of follow-up was 12.2 months in the pregnant with gMG cohort, 12.6 months in the pregnant without MG cohort, and 12.0 months in the non-pregnant with gMG cohort.

Pregnancy outcomes

The majority of women in both pregnant cohorts reached the second trimester (62.9% in the pregnant with gMG cohort and 69.8% in the pregnant without MG cohort).

Rates of live birth were not statistically different between cohorts (pregnant with gMG: 58.8% vs. pregnant without MG: 64.3%; Fig. 1), as were rates of spontaneous abortion (21.6% vs. 23.4%), ectopic pregnancy (2.1% vs. 1.7%), stillbirth (0.0% vs. 0.5%), and unclassified deliveries (4.1% vs. 3.2%). There was a non-significant ($p = 0.068$) trend towards more induced abortions in the pregnant with gMG vs. pregnant without MG cohorts (13.4% vs. 7.0%). Preterm birth was 2.5 times more frequent in the pregnant with gMG cohort vs. the pregnant without MG cohort (21.1% vs. 9.6%; OR: 2.50, $p = 0.021$). Rates of extreme preterm birth (25.0% vs. 11.4%; OR: 2.37, $p = 0.217$), very preterm births (8.3% vs. 11.1%; OR: 0.75, $p = 0.801$) or moderate-to-late-preterm births (66.7% vs. 77.5%; OR: 0.58, $p = 0.443$) did not differ significantly. Pregnant women with gMG were 2.64 times more likely to undergo Cesarean section than the pregnant without MG cohort (21.1% vs. 10.0%; OR: 2.64, $p = 0.006$).

Among live births, the mean gestational age was significantly shorter in the pregnant with gMG cohort compared to the pregnant without MG cohort (37.0 weeks vs. 38.2 weeks; mean difference: 1.2 weeks, $p = 0.008$).

Exacerbation and crisis

During follow-up, rates of MG exacerbations were similar between pregnant with gMG and non-pregnant with gMG cohorts (35.1% vs. 30.2%, OR: 1.25, $p = 0.391$; Fig. 2). However, pregnant women with gMG were more likely to experience an MG crisis (3.1% vs. 0.8%, OR: 3.9, $p = 0.027$). Within the pregnant with gMG cohort, there were on average 1.8 MG-related clinical events (i.e., exacerbation and crisis) in the first

trimester (exacerbation: 1.8; crisis: 0.0), 3.7 events in the second–third trimester (3.7; 0.0), and 3.1 events in the postpartum period (3.1; 0.0).

Use of gMG-related therapies

During the follow-up period, gMG-related medication use was generally similar between the pregnant with gMG and the non-pregnant with gMG cohorts (AChE inhibitors: 68.0% vs. 65.5%; systemic corticosteroids: 49.5% vs. 50.7%; systemic corticosteroids with mean daily prednisone-equivalent dose > 10 mg/day: 22.7% vs. 22.1%; immunoglobulin: 23.7% vs. 24.0%). The uses of C5i (3.1% vs. 5.5%) and FcRn blockers (0.0% vs. 1.6%) were low in both cohorts. Use of immunosuppressants was significantly lower in the pregnant with gMG cohort (17.5% vs. 33.6%; OR: 0.42, $p = 0.004$). The pregnant with gMG cohort had fewer days per month with supply of non-steroidal immunosuppressants (mean difference: -4.0 days, $p < 0.001$; Fig. 3), rituximab (mean difference: -1.5 days; $p < 0.001$), and C5i (mean difference: -1.1 days, $p < 0.001$) compared to the non-pregnant with gMG cohort.

Almost a quarter of the pregnant with gMG cohort (23.7%; **Supplementary Table S3**) used medications or underwent procedures not recommended during pregnancy, predominantly non-steroidal immunosuppressants (i.e., azathioprine, mycophenolate, methotrexate; 69.6%), rituximab (17.4%), and thymectomy (13.0%). These largely occurred during the first trimester.

HRU and healthcare costs

Compared with the pregnant without MG cohort, the pregnant with gMG cohort exhibited similar numbers of inpatient days and ER visits, but 1.81 times the number of outpatient visits per month ($p < 0.001$; Fig. 4). Mean monthly all-cause total healthcare costs were \$3,170 higher in the pregnant with gMG cohort than the pregnant without MG cohort ($p < 0.001$; Fig. 5), a difference primarily attributable to pharmacy costs (\$2,290; $p < 0.001$). Pregnancy-related HRU and cost patterns were similar among the two pregnant cohorts.

Compared with the non-pregnant with gMG cohort, the pregnant with gMG cohort had 2.94 times the number of gMG-related inpatient admissions per month ($p < 0.001$; Fig. 4), while the number of outpatient and ER visits were similar. Mean monthly gMG-related total healthcare costs were \$2,985 lower in the pregnant with gMG cohort ($p = 0.020$; Fig. 5), driven primarily by \$3,483 lower pharmacy costs ($p = 0.008$), including lower costs for immunoglobulin (pregnant with gMG: \$1,645 vs. non-pregnant with gMG: \$2,664, $p = 0.275$), C5i (\$427 vs. \$2,736, $p < 0.001$), rituximab (\$35 vs. \$94, $p = 0.112$), and FcRn blockers (\$0 vs. \$89, $p < 0.001$). Mean monthly gMG-related medical costs were \$482 higher in the pregnant with gMG cohort ($p = 0.024$) due to \$384 higher inpatient costs ($p < 0.001$).

DISCUSSION

The findings from this retrospective cohort study highlight the bidirectional challenges of managing pregnancy in the context of gMG and, conversely, managing gMG in the context of pregnancy. Obstetric complications were more frequent in pregnant women with gMG, including higher rates of prematurity and Cesarean delivery compared with pregnant women without MG. Pregnant women with gMG received fewer

medications to control MG, experienced a comparable rate of MG exacerbations and, although rare, a higher rate of MG crisis relative to non-pregnant women with gMG. The reduction in treatment utilization was reflected in substantially lower gMG-related pharmacy costs.

Our findings regarding adverse pregnancy outcomes associated with gMG are consistent with prior literature [35, 36], which has suggested that neuromuscular weakness, fatigue, and respiratory compromise in gMG may contribute to obstetric complications [37]. Muscle weakness of the abdominal and pelvic floor musculature may impair expulsive effort during labor [38, 39], increasing the likelihood of assisted deliveries, including Cesarean section [12, 36].

Previous studies from Norway and Sweden have shown higher rates of elective Cesarean sections and similar rates of emergency Cesarean sections among pregnant women with gMG compared to those without, suggesting that expectation of risk may drive the decision to undergo this procedure [40, 41]. Concerns related to respiratory function under the stress of labor may also prompt clinicians to opt for surgical delivery as a precautionary measure [36]. There has also been a trend toward a greater reliance on Cesarean section among obstetricians, although not entirely based on clinical necessity, but preference and concern for complications [42]. However, international consensus guidance for MG management recommends spontaneous vaginal delivery as the preferred approach when feasible and should be actively encouraged [13]. This underscores the need for clearer guidance and education to help clinicians to better distinguish scenarios in which Cesarean section is medically indicated vs. when vaginal delivery remains a safe and appropriate option.

The observed under-utilization pattern of gMG-specific treatments during pregnancy highlights the need to strengthen evidence-based treatment decision-making for this population. A multidisciplinary approach involving both neurology and obstetrics teams should be focused on managing MG disease activity during pregnancy while minimizing fetal and maternal risks. Despite the relatively low utilization of gMG treatments during pregnancy overall, approximately one quarter of pregnant women with gMG received treatments contraindicated in pregnancy, most often in the first trimester, potentially before pregnancy recognition. These findings reinforce the need for safe, accessible MG treatments suitable for women who are pregnant or may become pregnant. Addressing this gap could improve disease control and reduce the risk of complications for both mother and infant.

Future research should explore potential drivers of increased adverse pregnancy outcomes among women with gMG and examine how pre-pregnancy disease course and severity influence treatment decisions and outcomes during pregnancy. It will be important to determine whether elevated risks of preterm and shorter gestational age are primarily attributable to gMG itself, to treatments, to interactions with comorbidities, or to demographic and socioeconomic factors. Subgroup analyses comparing pregnant women with well controlled gMG vs. those with recent exacerbations or crises may provide valuable insight into real-world clinical decision-making and could inform future guidelines for gMG management during pregnancy.

Key strengths of this study include the use of a large, real-world U.S. administrative claims database, which captures a diverse population across multiple payer types. The extended observation period, from pre-

pregnancy through six months postpartum, enabled a comprehensive assessment of both the clinical and economic impact of gMG during and after pregnancy. Inclusion of two comparison groups (pregnant women without MG and non-pregnant women with gMG) allowed the study to provide valuable context to differentiate the effects of pregnancy from the underlying disease burden of gMG, offering a clearer understanding of how gMG interacts with pregnancy. The study also identified notable treatment gaps, particularly the under-utilization of advanced therapies among both the pregnant and non-pregnant gMG cohorts, which may inform clinical decision-making and highlight areas for future research aimed at optimizing care for women who are pregnant or may become pregnant.

LIMITATIONS

The findings of this study should be interpreted in light of several important limitations. First, due to the lack of a specific ICD-10-CM diagnostic code for gMG, identification relied on a claims-based algorithm incorporating MG diagnosis codes, healthcare settings, and provider specialties. Second, the use of administrative claims data is inherently dependent on accurate coding of diagnoses, procedures, and medications. Inaccuracies or inconsistencies in coding may result in misclassification or misidentification of cases. Furthermore, individual claims can include multiple diagnosis codes, making it difficult to attribute HRU or costs exclusively to a single condition (e.g., claims that include both pregnancy and MG codes may be counted as related to both pregnancy and gMG). Third, while weighting methods were applied to balance the comparison groups, residual confounding may still be present due to unmeasured variables such as lifestyle factors, socioeconomic status, or availability of social support. In addition, matching the pregnant cohorts on length of follow-up may have inadvertently resulted in more similar pregnancy durations, potentially making pregnancy outcomes appear more alike. Despite this possible bias, differences in pregnancy outcomes were still observed. These limitations, combined with the observational design of the study, limit the ability to draw causal inferences. Fourth, the findings may not be generalizable to populations outside the study sample, such as individuals without health insurance or those covered by insurance plans other than commercial, Medicare Advantage, or Medicaid. Lastly, the use of certain medications, particularly advanced therapies, was relatively uncommon in the study population, which could be partially due to the recency of available data; future studies are needed to better understand the use of these medications in pregnant women with gMG.

CONCLUSIONS

In conclusion, gMG presents ongoing challenges for women and clinicians during both pregnancy and the postpartum period, with a higher risk of adverse obstetric outcomes and MG clinical events. This study adds to the growing body of evidence showing that women with gMG face a higher risk of preterm delivery and increased rates of Cesarean section. At the same time, despite the elevated risk for MG crisis, our findings indicate that pregnant women receive less immunosuppressive treatment and incur lower costs for gMG treatment. These gaps in care highlight the critical need for closer clinical monitoring and more proactive treatment strategies during pregnancy.

Abbreviations

AChE	Acetylcholinesterase
C5i	C5 inhibitor
CI	Confidence interval
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
ER	Emergency room
FcRn	Neonatal Fc receptor
gMG	Generalized myasthenia gravis
HIPAA	Health Insurance Portability and Accountability Act
HRU	Healthcare resource utilization
ICD-9-CM	International Classification of Diseases, 9 th Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, 10 th Revision, Clinical Modification
KRD+	Komodo Research Data
MCD	Mean cost difference
MD	Mean difference
MG	Myasthenia gravis
N/A	Not applicable
OLS	Ordinary least squares
OR	Odds ratio
RR	Rate ratio
SD	Standard deviation
Std. diff.	Standardized difference
U.S.	United States

Declarations

Funding

This study was funded by Johnson & Johnson. The study sponsor was involved in several aspects of the research, including the study design, interpretation of data, and writing of the manuscript.

Competing interests

LJ, JP, MJ, and ZC are employees and stockholders of Johnson & Johnson. MZ, PB, ATS, FL, DP, and BL are employees of Analysis Group ULC, a consulting company that has provided paid consulting services to Johnson & Johnson, which funded the development and conduction of this study.

Authors' contributions

All authors have made substantial contributions to the conception or design of the study, or the acquisition, analysis, or interpretation of data, drafting the manuscript and revising it critically for important intellectual content, and have provided final approval of this version to be published and agree to be accountable for all aspects of the work.

Availability of data and materials

The data that support the findings of this study are available from the KRD+ database. Restrictions apply to the availability of these data, which were used under license for this study.

Ethics statement and consent to participate

Data were de-identified and comply with the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996; therefore, no review by an institutional review board was required per Title 45 of CFR, Part 46.101(b)(4) (<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.101>).

Consent for publication

Not applicable.

Acknowledgements

Not applicable.

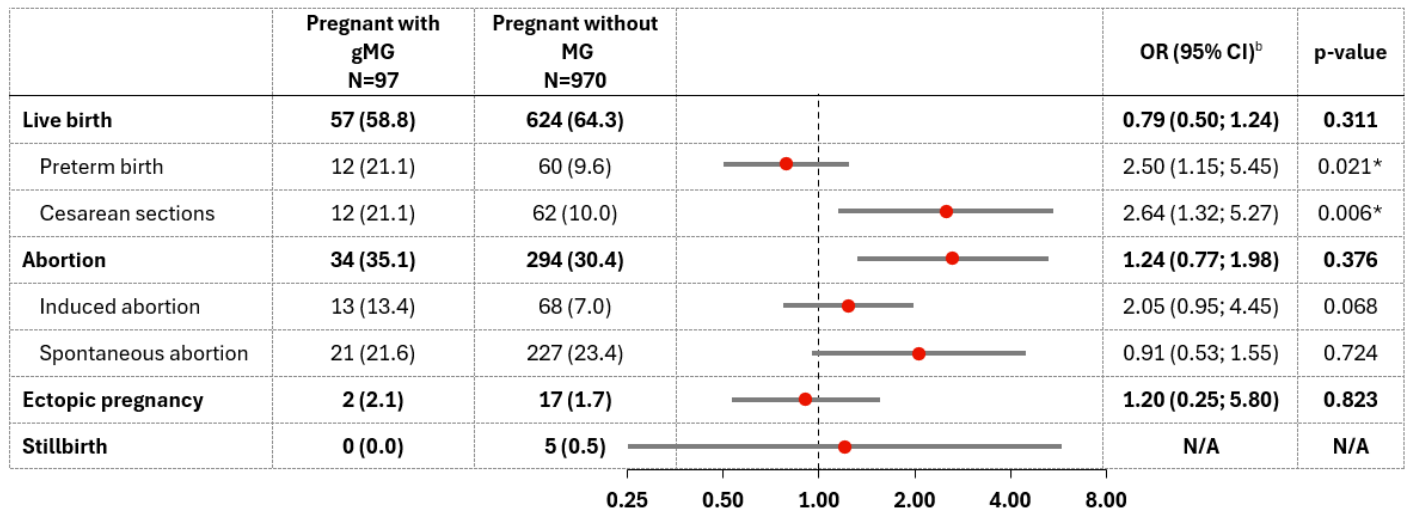
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Figures



Abbreviations: CI = confidence interval; gMG = generalized myasthenia gravis; MG = myasthenia gravis; N/A = not applicable; OR = odds ratio.

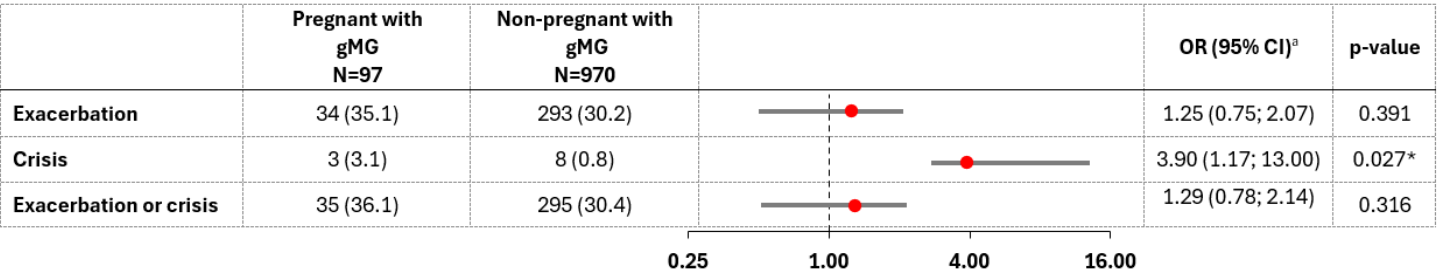
* denotes p-value <0.05.

Notes:

- Results did not include those with unknown pregnancy outcomes.
- ORs were estimated using logistic regression models. An OR >1 indicates that the pregnant with gMG cohort had higher odds of having an outcome compared to the pregnant without MG cohort.

Figure 1

Pregnancy outcomes during follow-up period^a



Abbreviations: CI = confidence interval; gMG = generalized myasthenia gravis; MG = myasthenia gravis; OR = odds ratio.

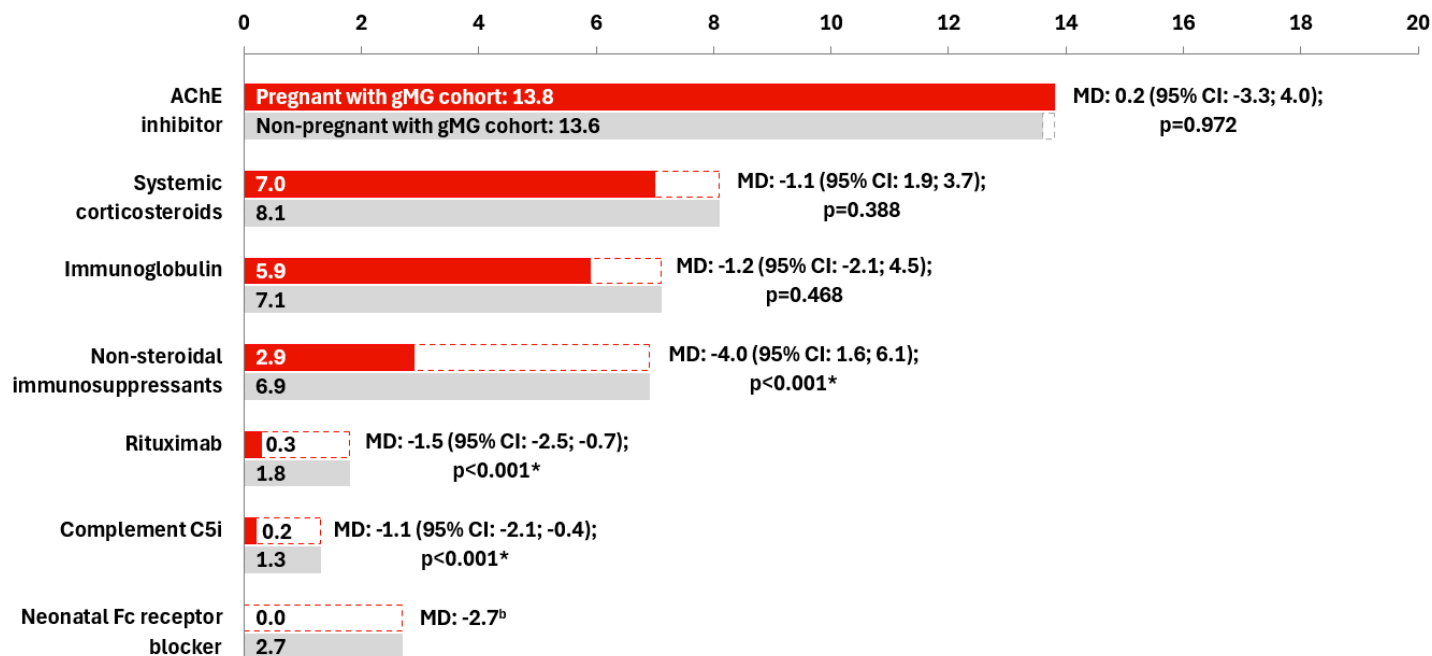
* denotes p-value <0.05.

Notes:

- ORs were estimated using logistic regression models. An OR >1 indicates that the pregnant with gMG cohort had higher odds of having an encounter compared to the non-pregnant with gMG cohort.

Figure 2

MG exacerbations and crises during follow-up period



Abbreviations: AChE = acetylcholinesterase; C5i = C5 inhibitor; CI = confidence interval; gMG = generalized myasthenia gravis; MD = mean difference; OLS = ordinary least squares.

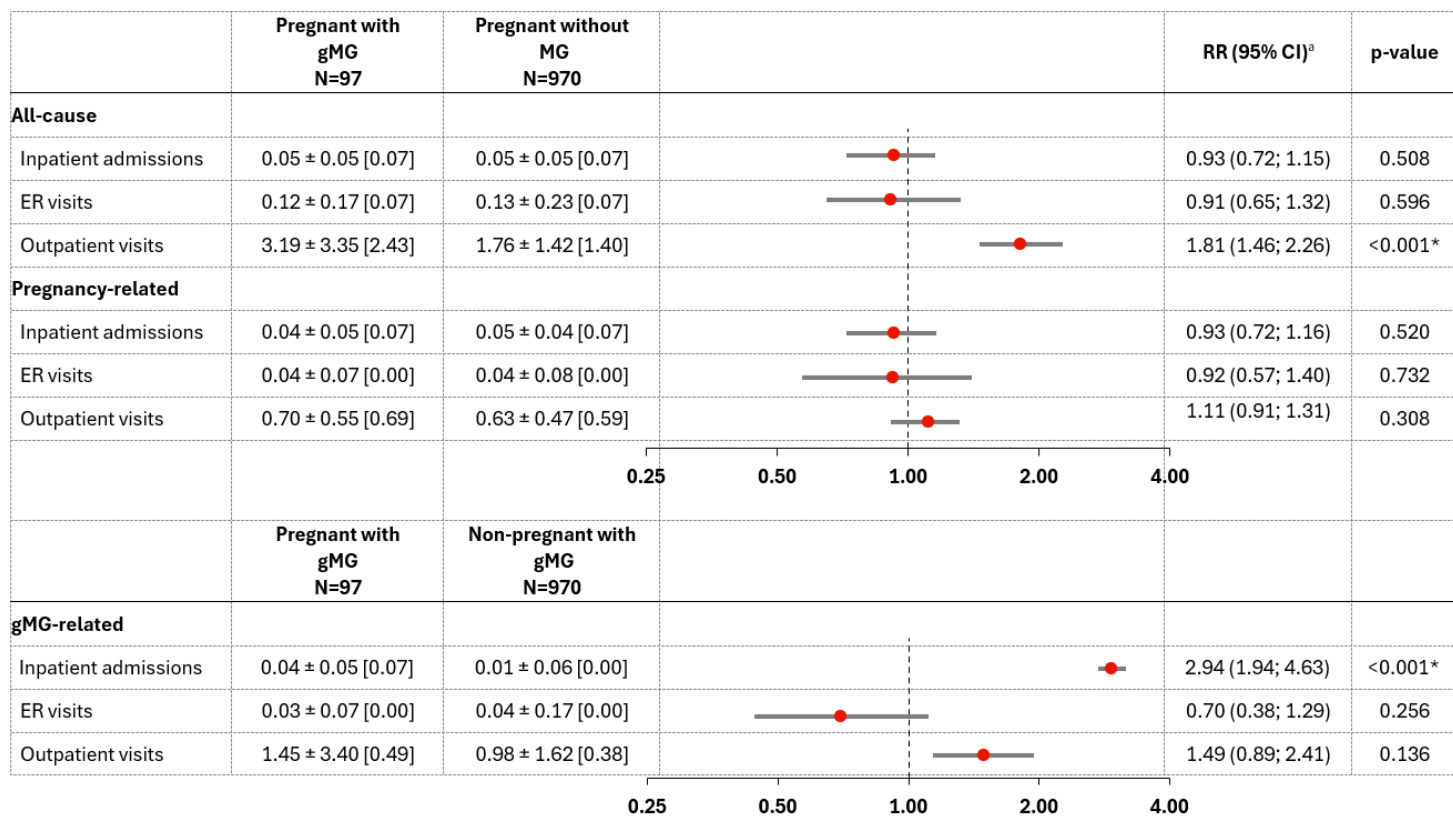
* denotes p-value <0.05.

Notes:

- MDs were estimated using OLS regression models; a non-parametric bootstrapping procedure was used to produce 95% CIs and p-values using OLS regression models. An MD >1 indicates that the pregnant with gMG cohort had higher days of supply compared to the non-pregnant with gMG cohort.
- There were no claims for FcRn blockers in the pregnant with gMG cohort during follow-up.

Figure 3

Mean monthly days of supply for gMG-related treatments during follow-up period^a



Abbreviations: CI = confidence interval; ER = emergency room; HRU = healthcare resource utilization; MG = myasthenia gravis; RR = rate ratio.

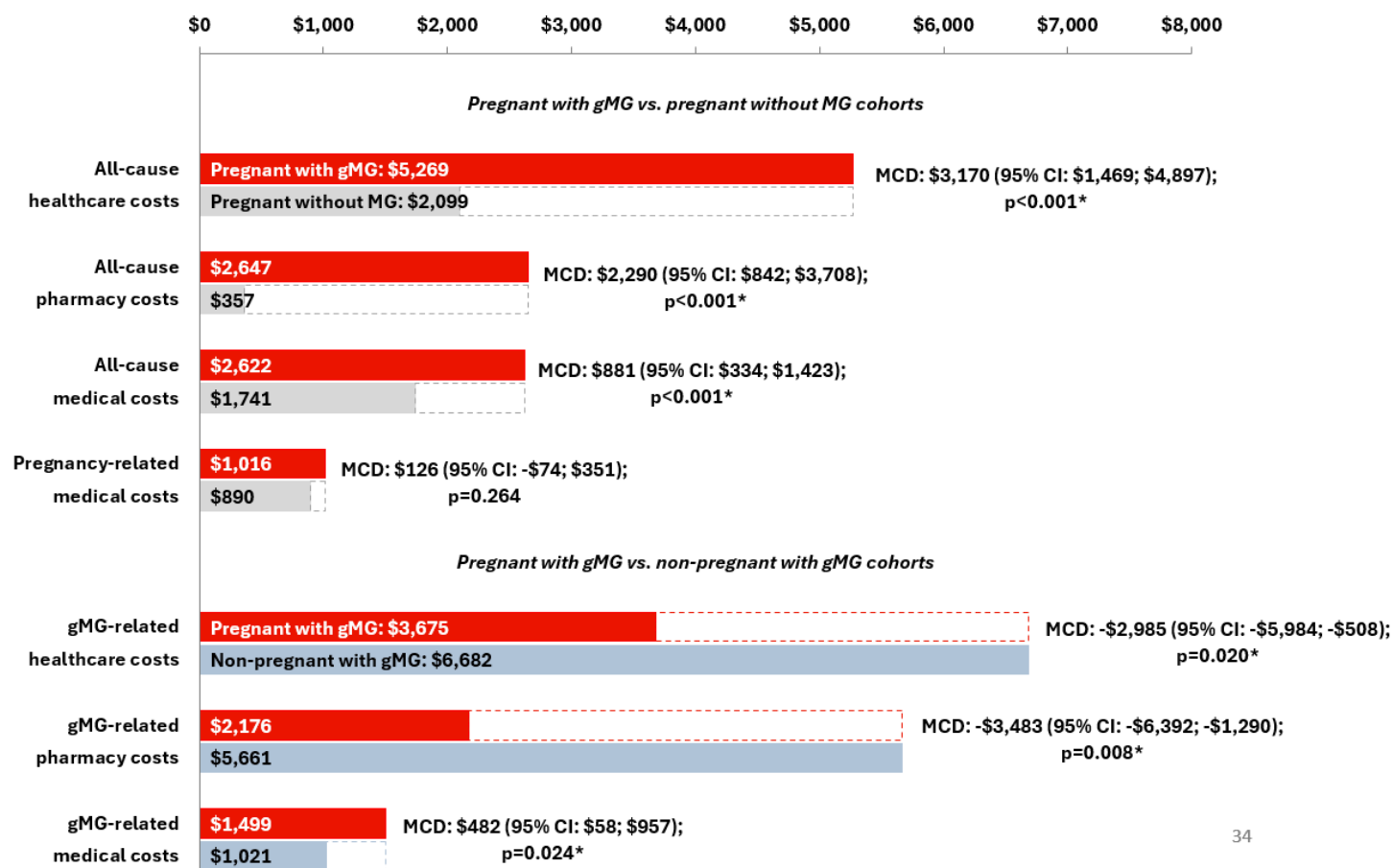
* denotes p-value <0.05.

Note:

- a. RRs were estimated using Poisson regression models; a non-parametric bootstrapping procedure was used to produce 95% CIs and p-values using Poisson regression models. An RR >1 indicates that the pregnant with gMG cohort had a higher rate of having the outcome compared to the control cohorts.

Figure 4

Monthly HRU during follow-up period^a



Abbreviations: CI = confidence interval; gMG = generalized myasthenia gravis; MCD = mean cost difference; MG = myasthenia gravis; OLS = ordinary least squares.

* denotes p-value <0.05.

Note:

- MCDs were estimated using weighted OLS regression models; a non-parametric bootstrapping procedure was used to produce 95% CIs and p-values using OLS regression models. For pregnant with gMG vs. non-pregnant with gMG cohorts, the OLS regression models were further adjusted for comorbidities that remained unbalanced after weighting (i.e., anxiety disorders, depressive disorders, dysphagia, fluid and electrolyte disorders, general and other muscle-specific weakness and other neurological condition).

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Figure 5

Mean monthly healthcare costs during follow-up period^a

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