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ORIGINAL ARTICLE

Myasthenia gravis and pregnancy: retrospective evaluation of 27 pregnancies in a tertiary center and comparison with previous studies

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Abstract

Background and aim To share our experience with the management of pregnancies in women with myasthenia gravis (MG) in a tertiary center.

Methods The study retrospectively evaluated 27 pregnancies in 12 patients. The pregnancies were divided into 3 groups on the basis of the clinical course of MG during pregnancy: improvement ($n = 7$), disease-stable ($n = 9$), and deterioration ($n = 11$). The groups were compared with respect to patient characteristics, clinical features, and obstetric outcomes.

Results There were 4 miscarriages (14.8%), 3 preterm births (11.1%), and 4 cases of preterm premature rupture of the membranes (PPROM) (14.8%). Exacerbation was observed in 25.9% of the cases; the remission rate during the postpartum period and after miscarriage was 37%. The cesarean section (CS) rate was 78.3%. Pregnancies with deterioration of MG were statistically more likely to have higher miscarriage, preterm birth, PPROM, CS, and transient neonatal MG rates, in addition to a lower gestational age at birth, birth weight, and 5-min Apgar score than pregnancies with improved or stable disease (p values < 0.001, 0.04, 0.03, 0.009, 0.02, < 0.001, 0.002, and 0.043, respectively).

Conclusion Physicians who manage pregnant women with MG must be familiar with the clinical features of the condition; a multidisciplinary approach is necessary for a better prognosis.

Keywords Acetylcholine receptors · Myasthenia gravis · Neuromuscular junction · Obstetric complications · Pregnancy

Introduction

Myasthenia gravis (MG) is an autoimmune disease that causes fluctuating weakness in the ocular, bulbar, limb, and respiratory muscles because of an antibody-mediated immunological attack on the acetylcholine receptors (AChRs) at the neuromuscular junction [1].

The incidence of MG ranges from 7 to 23 new cases per million and the estimated prevalence is 70 to 320 per million [2, 3]. Although MG can occur in any age group, it is more common in women in the second and third decades of life [2, 4]. Therefore, MG might complicate pregnancies, mainly because of its epidemiologic characteristics; physicians should be familiar with the management protocols during the peripartum period.

There are 2 clinical types of MG: (1) ocular and (2) generalized [5]. Diagnosis of MG is chiefly based on the clinical diagnosis, supported by the patient's history, physical examination, and various ancillary tests (ice pack test, edrophonium test, autoantibody serology, and electrodiagnostic studies) [6]. Autoantibodies against AChR, muscle-specific receptor tyrosine kinase (MuSK), and other postsynaptic neuromuscular junction components play a pivotal role in the development of MG [5].

MG progresses with relapses and remissions; the clinical status of the disease and its severity are assessed using several classifications/scoring systems. The Myasthenia Gravis Foundation of America (MGFA) Clinical Classification, MGFA post-intervention Status Classification, and MG Composite (MGC) Score are the most frequently used systems for this purpose [7].

Treatment protocols consist of symptomatic management with anticholinesterase agents; immunomodulation with glucocorticoids/immunosuppressive drugs and

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plasmapheresis/intravenous immune globulin (IVIG); and thymectomy for patients with thymoma and/or seropositive generalized MG [8].

Pregnancy has varying effects on MG prognosis, exacerbation, and remission; there may be no change in disease status during pregnancy [9]. In contrast, postpartum exacerbation occurs in approximately 30% of patients [10–13]. The first trimester and early postpartum period have the highest risk for disease exacerbation [14]. Exacerbation may also be associated with abortion [10, 11]. Transient neonatal MG (TNMG) develops as a result of transplacental passage of AChR IgG antibodies in 10–20% of infants born to mothers with MG [15]. Prenatal counseling should be provided to all MG patients for clinical management of the disease and to avoid teratogenic medications through multidisciplinary healthcare efforts. Furthermore, follow-up of these patients should be conducted at tertiary centers with adequate facilities [7, 14, 16]. Preterm labor, preterm premature rupture of membranes (PPROM), and rates of cesarean section (CS) are reportedly higher in pregnancies with MG [17, 18]. Labor and delivery are other areas of concern, as the second stage of labor might be affected by MG [10–13]. Labor analgesia/anesthesia is another important concern as anesthesia-related complications are more frequent in patients with MG [17, 19]. Close follow-up with special care in the first 48 to 72 h of life is recommended if physical examination of the newborn raises a suspicion of TNMG [14]. Proper treatment protocols should be established for postpartum exacerbation, and medication should be prescribed according to breastfeeding status [9, 14].

The aim of this study was to evaluate clinical characteristics, gestational outcomes, and obstetric complications in patients with MG at our institution.

Materials and methods

This study retrospectively evaluated the clinical characteristics, gestational outcomes, and obstetric complications in patients with MG who were followed up at the Hacettepe University Hospital, Division of Perinatology between January 1, 2010, and December 31, 2017. Hacettepe University Hospital is a public tertiary referral center located in the capital city of Turkey; it serves patients from all over the country. The required data were obtained from the Hacettepe University Perinatal Medicine database. Pregnant women with a preexisting diagnosis of MG were included in the study.

The diagnosis of MG was established by the physicians of the Hacettepe University Hospital Department of Neurology based on the clinical findings, electrophysiologic confirmatory tests, disease-specific antibodies, and improvement of symptoms after administration of acetylcholinesterase inhibitors or immunosuppressive drugs [1, 7]. Preconception counseling was provided to all patients. All pregnancies were followed up within the framework of a special antenatal care program for MG. Neurological examination was performed by neurologists during the preconception period, pregnancy (during each trimester), and the postpartum period. Thus, depending on the pregnancy outcome, 3 to 5 neurological examinations were performed. Patients were followed up during the first year after delivery. Screening pulmonary function tests were performed for each pregnancy. Disease severity was assessed according to the MGFA Clinical Classification, MGFA post-intervention Status Classification, and MGC Score at each visit. The MGFA Clinical Classification divides patients into 5 classes: class I includes only those with isolated ocular muscle weakness, while class V includes the most severe cases that require intubation [7]. The MGFA post-intervention Status Classification evaluates patients in terms of the clinical course of the disease, symptom progression, and medications used [7]. The MGC Score is based on physical examination and patient history [7]. Medications were adjusted based on clinical findings, patient complaints, and disease severity [1, 7]. Pregnancy follow-up consisted of serial laboratory examinations and ultrasonography, aneuploidy screening (combined or triple test), fetal anatomy scanning at 20–24 weeks of gestation, an oral glucose challenge test, and a non-stress test (after gestational week 28). The pregnancies were divided into 3 groups based on the status of MG: (1) improvement group (substantial decrease in pretreatment clinical manifestations or sustained substantial reduction in medication), (2) disease-stable group (no substantial change in pretreatment clinical manifestations or reduction in medications), and (3) deterioration group (substantial increase in pretreatment clinical manifestations or a substantial increase in medications) [1, 7]. TNMG was diagnosed by neonatologists on the basis of clinical signs in the newborn (generalized hypotonia, weak cry, hyporeflexia, impaired sucking, or respiratory difficulty) [14].

Maternal age, body mass index (BMI) (kg/m^2), obstetric history (gravidity, parity, miscarriages, live births), MG type (generalized, ophthalmic), disease duration since diagnosis (months), antibody positivity and type (anti-AChR, anti-MuSK, seronegative), history of thymectomy, obstetric complications (miscarriage, preterm labor, PPROM), medications (pyridostigmine, prednisolone, IVIG, etc.), route of delivery, spontaneous/induced labor rates, length of labor, CS characteristics (pre-labor CS rates, CS at labor stages, CS indications), gestational week at birth, birth weight, labor anesthesia, 5-min Apgar score, TNMG, breastfeeding initiation/maintenance rates (at postpartum 6 months), and exacerbation/remission of the disease in the postpartum period were compared among the groups. Disease severity during the antepartum, intrapartum, and postpartum periods was also evaluated [7].

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY, USA).

Variables were investigated using visual (histograms, probability plots) and analytical methods (Shapiro-Wilk test) to determine whether data were normally distributed. Descriptive analyses were presented as medians and interquartile ranges for the non-normally distributed variables. As continuous variables were not normally distributed, the Kruskal-Wallis test was conducted to compare the median values among the groups. The Mann-Whitney *U* test was performed to test the significance of pairwise differences, using the Bonferroni correction to adjust for multiple comparisons. An overall 5% type-I error level was used to infer statistical significance. Categorical variables were presented as numbers and percentages. The chi-square test was used to compare categorical variables among the groups. A 2-tailed p value < 0.05 was regarded as statistically significant. The study protocol was approved by the Hacettepe University Ethics Committee (GO 17/425). Owing to the retrospective design of the study, the need for patient consent was waived.

Results

Among 16,320 pregnancies between January 1, 2010, and December 31, 2017, 12 women had MG; these patients accounted for 27 pregnancies (0.16%, all singletons). One patient had 5 pregnancies (2 miscarriages, 3 with PPROM), 1 had 4 pregnancies (1 miscarriage, 1 preterm, 2 term births), 2 had 3 pregnancies (1 with PPROM, 2 term births, 1 preterm, 2 term births respectively for each), 4 patients had 2 pregnancies (1 miscarriage and 1 term birth for the first, 1 preterm and 1 term birth for the second, 2 term births for the third, and 1 preterm and 1 term births for the fourth patient), and 4 patients had 1 pregnancy (all were term births).

Clinical characteristics and gestational outcomes of the 27 pregnancies are shown in Tables 1 and 2. The median maternal age and BMI were 29 years and 23.4, respectively. The median disease duration since the diagnosis of MG was 36 months. Generalized MG was present in 22 pregnancies (81.5%), with ocular MG in 5 pregnancies (18.5%) (1 patient with 3 pregnancies and 2 patients with 1 pregnancy each). All pregnancies had a positive autoantibody test (20 anti-AChR and 7 anti-MuSK). Four patients were anti-MuSK positive (1 patient with 3, 1 patient with 2, and 2 patients with 1 pregnancy). Seven pregnancies in 4 patients were post-thymectomy (25.9%). There were 4 miscarriages (4/27) (14.8%), 3 preterm births (3/27) (11.1%), and 4 cases of PPROM (4/27) (14.8%). The median gestational age at birth and birth weight were 38 weeks and 3030 g, respectively. The median 5-min Apgar score was 10. Among the 23 deliveries, 5 (21.7%) were vaginal and 18 (78.3%) were cesarean births (CS). General anesthesia/analgesia was administered for 6 deliveries (26%) and regional anesthesia/analgesia was administered for 17 deliveries (74%). TNMG was observed in 6 infants (26%). MG was exacerbated in 7 (26%) pregnancies during the postpartum period and after miscarriage. In contrast, disease remission was observed in 10 pregnancies during the postpartum period and after miscarriage (37%).

There were 7, 9, and 11 pregnancies in the improvement (26%), disease-stable (33.3%), and deterioration groups (4 first trimester, 5 s trimester, and 2 third trimester exacerbations) (40.7%), respectively. Corticosteroid therapy was used for all patients in the deterioration group. Immunomodulating drugs, plasmapheresis, and IVIG were not used for the exacerbations. Comparisons of the groups in terms of patient characteristics, clinical features, and obstetric outcomes (median-interquartile range, percentiles, p values) are shown in Table 3.

Pregnancies with deterioration of MG were statistically more likely to have higher miscarriage, preterm birth,

Table 1 Demographic and obstetric data of individuals

Maternal age[a]	29 (4)
BMI[a]	23.40 (0.50)
Gravidity[a]	2 (1)
Parity[a]	0 (1)
Number of previous miscarriages[a]	0 (1)
Living child[a]	0 (1)
Disease duration since the diagnosis of MG (months)[a]	36 (24)
Gestational week at birth[a]	38 (3.90)
Birth weight (g)[a]	3030 (870)
5th minute APGAR Score[a]	10 (2)

[a] Median (interquartile range)

BMI body mass index, *MG* myasthenia gravis

Table 2 Miscarriage, preterm birth, PPROM, pregestational thymectomy, vaginal delivery, CS, general/regional anesthesia/analgesia, TNMG, and postpartum/miscarriage exacerbation/remission rates for 27 pregnancies

Variables (n, %)	Percentages
Ocular disease	5 (18.5%)
Generalized disease	22 (81.5%)
Anti-AChR positivity	20 (74%)
Anti-MuSK positivity	7 (26%)
Pregestational thymectomy	7 (26%)
Vaginal delivery	5 (21.7%)
CS	18 (78.3%)
General anesthesia/analgesia	6 (26%)
Regional anesthesia/analgesia	17 (74%)
TNMG	6 (26%)
Postpartum/miscarriage exacerbation	7 (26%)
Postpartum/miscarriage remission	10 (37%)

MG myasthenia gravis, *PPROM* preterm premature rupture of membranes, *CS* cesarean section, *TNMG* transient neonatal MG

Table 3 Comparison of the MG improvement, disease-stable, and deterioration groups within the frame work of patient characteristics, clinical features, and obstetric outcomes

Variables	Improvement group ($n = 7$)	Disease-stable group ($n = 9$)	Deterioration group ($n = 11$)	p value
Maternal age[a,b]	28 (2)	31 (7)	29 (5)	0.30
BMI[a,b]	23.40 (0.50)	23.70 (0.80)	23.30 (0.50)	0.44
Ocular MG[c,d]	14.2% (1/7)	33.3% (3/9)	9% (1/11)	0.37
Anti-MuSK positivity[c,d]	57.1% (4/7)	33.3% (3/9)	0% (0/7)	0.07
Gravida[a,b]	1 (1)	2 (2)	1.5 (2)	0.71
Parity[a,b]	0 (1)	1 (1)	0 (1)	0.65
Number of previous miscarriages[a,b]	0 (0)	0 (0)	0.5 (1)	0.70
Living child[a,b]	0 (1)	1 (1)	0 (1)	0.65
Disease duration since the diagnosis of MG (months)[a,b]	24 (12)	48 (24)	24 (30)	0.31
Miscarriage rate[c,d]	0% (0/7)	0% (0/9)	36.4% (4/11)	$p < 0.001$
Preterm birth rate[c,d]	14.3% (1/7)	0%(0/9)	18.2%(2/11)	$p = 0.04$
PPROM rate[c,d]	0% (0/7)	0% (0/9)	45.5% (5/11)	$p = 0.03$
Pregestational thymectomy rate[c,d]	42.8% (3/7)	33.3% (3/9)	9% (1/11)	$p = 0.16$
Rate of spontaneous labor[c,d]	71.4% (5/7)	55.5% (5/9)	57.1% (4/7)	0.12
Rate of induced labor [c,d]	28.6% (2/7)	44.5% (4/9)	42.9% (3/7)	0.12
Rate of spontaneous vaginal delivery[c,d]	100% (1/1)	N/A	50% (2/4)	0.26
Length of labor (minutes)[a,b]	480 (620)	120 (270)	480 (660)	0.23
CS rate[c,d]	85.7% (6/7)	100% (9/9)	42.8% (3/7)	$p = 0.009$
Pre-labor cesarean rate[c,d]	33.3% (2/6)	44.4% (4/9)	0% (0/3)	0.37
CS at stage of labor				0.54
First stage of labor	50% (3/6)	44.4% (4/9)	100% (3/3)	
Second stage of labor	16.6% (1/6)	11.1% (1/9)	0% (0/3)	
CS indications[c,d]				0.34
Previous CS	16.6% (1/6)	44.4% (4/9)	0% (0/3)	
Breech presentation	0% (0/6)	22.2% (2/9)	0% (0/3)	
CPD	16.6% (1/6)	11.1% (1/9)	0% (0/3)	
Macrosomia	16.6% (1/6)	11.1% (1/9)	0% (0/3)	
Fetal distress	16.6% (1/6)	11.1% (1/9)	66.6% (2/3)	
Lack of progress	33.3% (2/6)	0% (0/9)	33.3% (1/3)	
General anesthesia/analgesia rate for deliveries[c,d]	57.1%(4/7)	11.1%(1/9)	14.2%(1/7)	$p = 0.49$
Regional anesthesia/analgesia rate for deliveries[c,d]	42.9%(3/7)	88.9%(8/9)	85.8%(6/7)	$p = 0.50$
Gestational age at birth (weeks)[a,b]	38 (1)	38 (0)	34 (1)	$p < 0.001$
Birth weight (g)[a,b]	3100 (290)	3530 (775)	2520 (300)	$p = 0.002$
5-min APGAR Score[a,b]	10 (0)	10 (2)	8 (3)	$p = 0.043$
TNMG rate[c,d]	14.3% (1/7)	0% (0/9)	71.4% (5/7)	$p = 0.02$
Breastfeeding initiation rate[c,d]	85.7% (6/7)	77.7% (7/9)	71.4% (5/7)	0.81
Breastfeeding maintenance rate (at postpartum 6th month)[c,d]	66.6% (4/6)	57.1% (4/7)	60% (3/5)	0.71
Postpartum/miscarriage exacerbation rate[c,d]	57.1%(4/7)	22.2%(2/9)	9%(1/11)	$p = 0.22$
Postpartum/miscarriage remission rate[c,d]	0% (0/7)	33.3% (3/9)	63.6% (7/11)	$p = 0.25$

MG myasthenia gravis, *anti-MuSK*, anti-muscle-specific kinase antibody, *PPROM* preterm premature rupture of membranes, *CS* cesarean section, *TNMG* transient neonatal MG, *N/A* not applicable, *CPD* cephalopelvic disproportion

[a] Median (interquartile range)

[b] Kruskal-Wallis test was performed to calculate p values

[c] Frequency, *n*, %

[d] Chi-square test was performed to calculate *p* values

PPROM, CS, and TNMG rates, in addition to lower gestational age at birth, birth weight and, 5-min Apgar scores than pregnancies with improved or stable disease (p values were < 0.001, 0.04, 0.03, 0.009, 0.02, < 0.001, 0.002, and 0.043, respectively).

The miscarriage rate was statistically significantly higher in the deterioration group than in the other 2 groups ($p < 0.001$ for both). The preterm birth rate was higher in the deterioration and improvement groups than in the disease-stable group (p values were 0.034 and 0.04, respectively). The PPROM rate was statistically significantly higher in the deterioration group than in the other 2 groups ($p < 0.001$ for both). Although the CS rate was statistically significantly higher in the improvement and disease-stable groups than in the deterioration groups (p-values were $p < 0.001$ for both), no statistically significant difference was found between the groups in terms of spontaneous/induced labor, spontaneous vaginal delivery, length of labor, pre-labor CS rate, CS at labor stages, and CS indications. Instrumental delivery was not performed for any of the cases. However, the spontaneous labor rate was higher in the improvement group, and pre-labor CS was not performed for any case in the disease deterioration group. All CSs were performed for obstetric indications, and in-labor CSs were mostly performed during the first stage of labor. Previous CS, fetal distress, and failure to progress were the leading CS indications in this study. The TNMG rate was statistically significantly higher in the deterioration group than in the improvement and disease-stable groups (p values were 0.03 and 0.002, respectively). Pairwise comparisons revealed statistically significant differences between the deterioration and disease-stable groups as well as between the deterioration and improvement groups regarding the median gestational week at birth ($p < 0.001$ for both). Pregnancies with deterioration of MG had lower gestational age at birth compared to pregnancies with improved or stable disease. The differences in median birth weight between the deterioration group and other groups were also statistically significant (p values were 0.032 for the deterioration vs. improvement group and 0.002 for the deterioration vs. disease-stable group). Pregnancies with deterioration of MG had lower birth weights than pregnancies with improved or stable disease. Additionally, the difference in the median 5-min Apgar score between the deterioration and disease-stable groups was statistically significant ($p = 0.04$). Pregnancies with deterioration of MG had lower 5-min Apgar scores than pregnancies with stable disease. Breastfeeding initiation/maintenance and postpartum/miscarriage exacerbation rates were higher in the improvement group, while the postpartum remission rate was higher in the deterioration group. However, these findings were not statistically significant.

Discussion

MG is more common in women in the reproductive age group; therefore, understanding the relationship between MG and pregnancy is important for physicians. Limited data are available regarding the interaction between MG and gestation; the studies mostly consist of case series [11, 15, 18, 20–29]. The main goal of this study was to evaluate the clinical characteristics, gestational outcomes, and obstetric complications in patients with MG and to compare the results with data obtained from the current literature.

The median maternal age in this study (29 years) is consistent with that given in the literature, as MG is more predominant in women in the second and third decades of life [2, 3]. The overall median values for gravidity, parity, number of previous miscarriages, and live births are similar to those seen in previous studies [18, 22].

The course of MG varies throughout pregnancy [30]. The exacerbation rate of MG is reported to vary between 30 and 45% in various studies [11, 13, 30]. Disease exacerbation usually occurs during the first trimester and is observed less frequently in patients who have undergone pregestational thymectomy (especially in patients with thymoma) [1, 8, 10, 15]. Patients with controlled MG before pregnancy are less likely to develop exacerbation during pregnancy. However, physicians should be aware of the risk of postpartum exacerbations [10, 11, 13]. Seven pregnancies in 4 patients were post-thymectomy in our series (26%). There was only 1 post-thymectomy pregnancy in the disease deterioration group, compared to a total of 6 pregnancies in the disease-stable and remission groups. However, this difference was not statistically significant. We were unable to demonstrate anti-MuSK autoantibody positivity in the disease deterioration group. There was only 1 case with ocular involvement in the disease deterioration group.

Preterm delivery, PPROM, and CS rates are reported to be higher in MG patients [17, 18, 31]. In our series, the deterioration rate was 40.7% (11/27); these patients had the generalized form of disease (4 first trimester, 5 s trimester, and 2 third trimester exacerbations). Gestational age at birth, birth weight, and 5-min Apgar scores were found to be lower in the disease deterioration group than in the remission and disease-stable groups. Additionally, the rates of miscarriage (all 4 miscarriages occurred in the disease deterioration group), preterm birth (2 of 3 preterm deliveries were in the disease deterioration group), and PPROM (all 5 cases were in the disease deterioration group) were higher in the disease deterioration group than in the other groups. The higher rate of PPROM in the disease deterioration group may also be associated with the use of corticosteroids [32]. Expression of extracellular matrix proteins in human amnion epithelial cells and pituitary-adrenal axis hormones in fetal and maternal blood may be altered by corticosteroid administration, which may lead to PPROM, according to the results of various studies [33, 34].

Autoimmune antibodies, cell degradation products, and inflammatory cytokines are most likely responsible for injury to the vascular structures of the placenta and the cellular components of the maternal-fetal interface, resulting in placental inflammation. Altered biological events and immune system activation might result in impaired implantation and disturbed fetal perfusion [35–39]. Placental inflammation that leads to preterm labor may be the main etiology for the higher rate of adverse pregnancy outcomes in the disease deterioration group. Lower birth weight and Apgar scores in the disease deterioration group seemed to be associated with earlier gestational age at delivery in this study.

Labor, delivery, and anesthesia/analgesia may be challenging in pregnancies with MG as the course of the disease can affect these processes [10–13, 17–19]. Although CS may be necessitated more often because of obstruction in the second stage of labor due to weakness of the skeletal muscles and fatigue in pregnant women with MG, vaginal delivery is considered safe in the absence of severe complications and myasthenic crisis. Additionally, regional anesthesia/analgesia should be administered as general anesthesia/analgesia can cause severe complications such as malignant hyperthermia and prolonged necessitation for external ventilation [10–13, 17–19]. The CS rate was 78.3% in our study and regional anesthesia/analgesia was administered in 74% of cases, which is consistent with the numbers stated in the literature. The course of disease did not have a significant effect on the progress of labor in our cases. Cesarean section was performed for obstetric indications such as previous CS, fetal distress, cephalopelvic disproportion, breech presentation, and failure to progress in this study.

The TNMG rate in our study was 26%, which is also consistent with the literature [13, 15]; TNMG was more frequently seen in the newborns of patients in the deterioration group (71.4%). It is essential to provide appropriate support for these infants, especially in the early neonatal period.

Postpartum exacerbation of MG is a serious problem [15, 18]. In this study, the postpartum/miscarriage exacerbation and remission rates were 26% and 37%, respectively. The postpartum exacerbation rate in this study was slightly lower than that seen in previous studies [15, 26, 29] Physicians should be cautious during the postpartum period and inform patients about the likely exacerbation of MG. Neurology consultation must be provided before discharging the patient from the hospital. Additionally, mothers who need help for breastfeeding should be supported. The U.S. Department of Health and Human Services Healthy People 2020 goals aim to have 81.9% of infants initiate breastfeeding, with 60.6% continuing to breastfeed at 6 months, and 34% continuing to 1 year [40]. Although the difference was not statistically significant, the improvement group had the highest rates for both breastfeeding initiation and maintenance (85.7% and 66.6%, respectively). Thus, healthcare professionals should provide adequate care for patients with deterioration of MG during pregnancy to increase breastfeeding rates.

Our findings indicate that exacerbation of MG during pregnancy is associated with lower gestational age at delivery, birth weight, and 5-min Apgar scores, along with higher rates of miscarriage, preterm birth, PPROM, vaginal delivery, and TNMG. Route of delivery was found to be associated with obstetric indications rather than clinical course of the disease during pregnancy. Vaginal delivery may be preferred in appropriate cases. Further prospective studies are required to confirm the results of this study.

The strengths of this study are the long-term follow-up and the numerous parameters investigated. The limitations are the relatively small sample size and retrospective design.

In conclusion, physicians who manage pregnant women with MG must be familiar with the clinical features of the disease; a multidisciplinary approach is necessary for a better prognosis.

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Authors' contributions Atakan Tanacan: study design, collection of the data, statistical analysis, and manuscript writing; Erdem Fadiloglu: statistical analysis and manuscript writing; Gonca Ozten: collection of the data and manuscript writing; Ali Can Gunes: collection of the data and manuscript writing; Gokcen Orgul: literature review and manuscript writing; Mehmet Sinan Beksac: study design, review of the literature, and manuscript writing.

Compliance with ethical standards

Disclaimer The manuscript has not been published or submitted for publication elsewhere. All authors are in agreement with the content of this manuscript. Our study does not violate the policies and/or procedures established by this journal.

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The study was approved by the ethics committee of Hacettepe University on 05/16/2017: protocol number GO 17/425. The chairperson of the ethics committee is Professor Nurten Akarsu. The study was conducted in accordance with the Declaration of Helsinki.

Informed consent All patients gave informed consent for participation in the research study and patient privacy was protected.

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