

Mode of delivery and postpartum clinical relapse in women with multiple sclerosis: a retrospective cohort study from southern iran

 Maryam Poursadeghfard¹, Etrat Hooshmandi¹, Mahnaz Bayat¹, Mahsa Kalaei¹, Alireza Salehi^{2*} 

1. Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

2. Department of MPH, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

ABSTRACT

Introduction: Pregnancy-related disease activity in multiple sclerosis (MS) remains an important clinical concern. This study descriptively characterized postpartum relapses according to mode of delivery and described additional clinical, obstetric, and treatment-related characteristics.

Methods: This retrospective cohort study included women with MS who experienced pregnancy after MS diagnosis and were followed at a tertiary MS referral center in Southern Iran between 2024 and 2025. Postpartum relapse was defined as a new clinical relapse within three months after delivery. Because of the small number of relapse events and repeated pregnancies contributed by some women, analyses were restricted to descriptive statistics.

Results: A total of 83 pregnancy episodes from 26 women with MS were analyzed. Five postpartum clinical relapses (6%) occurred within three months after delivery. Relapses were observed across several delivery categories; however, the small number of events did not permit conclusions regarding an association between delivery mode and postpartum relapse. Deliveries followed by relapse showed higher mean EDSS scores and a greater descriptive frequency of some comorbidities, particularly hypothyroidism and diabetes mellitus. Pre-pregnancy disease-modifying therapy categories also showed different descriptive distributions between deliveries with and without relapse. No postpartum relapses occurred among deliveries associated with a relapse during the year before pregnancy or during pregnancy.

Conclusion: In this cohort, the descriptive distribution of postpartum relapse across delivery modes did not permit conclusions regarding an association. However, the limited number of relapse events warrants cautious interpretation, and larger prospective studies with standardized imaging follow-up are needed to evaluate these findings further.

Keywords:

Multiple sclerosis

Pregnancy

Postpartum period

Recurrence

Parturition

Introduction

Multiple Sclerosis (MS) is one of the most common

non-traumatic disabling neurological conditions affecting young adults (Dobson and Giovannoni 2019). Ap-

* Corresponding author: Alireza Salehi, salehialireza45@yahoo.com

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proximately 75% of individuals diagnosed with MS are women, with clinical symptoms typically beginning in early adulthood, coinciding with family planning. Research indicates that between 20% and 33% of women with MS have children after their diagnosis, making it essential to understand how maternal MS influences pregnancy outcomes for patients, families, and healthcare providers (van der Kop et al., 2011).

Historically, pregnancy was discouraged for women with MS, but recent studies suggest that it may have a beneficial effect on relapse rates without adversely affecting long-term disease progression (Koch et al., 2009). The landmark Pregnancy in MS (PRIMS) study challenged the notion that pregnancy is harmful to women with MS, revealing an increased risk of relapses during the first 3–4 months postpartum, particularly in those with highly active disease before conception (Varytè et al., 2021). One proposed explanation for the temporary remission of MS during pregnancy is a shift toward an anti-inflammatory immune state, along with changes in cellular and humoral immunity. Conversely, childbirth is associated with immune reconstitution and a return toward a more pro-inflammatory immune profile (Confavreux et al., 1998).

Several factors have been reported to predict an increased risk of relapse during the first three months following childbirth, including a higher relapse rate in the year before pregnancy, relapse activity during pregnancy, and a higher disability score at pregnancy onset (Vukusic et al., 2004). Few studies have investigated whether the mode of delivery or obstetric anesthesia influences postpartum disease activity. However, the impact of the mode of delivery on the rates of postpartum relapse is still not well understood. Some studies have suggested a possible association between cesarean delivery and increased relapse rates, potentially related to factors such as surgical stress and postpartum recovery (Schubert et al., 2023). At the same time, other studies show no notable difference (Pastò et al., 2012; Sadovnick et al., 2024). Gaining insight into this relationship is essential for making informed choices about delivery options for women with MS (Pastò et al., 2012).

Due to conflicting findings and limited data from Asian populations, we conducted a preliminary study to examine the association between mode of delivery and postpartum relapse in women with MS.

Material and Methods

Study population

This study was conducted as a retrospective cohort study at the MS Referral Clinic center affiliated with Shiraz University of Medical Sciences (SUMS) from May 2024 to March 2025. The target population comprised women with MS in southern Iran, and the study population included all women diagnosed with MS who attended the specialized MS clinic located in Imam Reza Clinic, also affiliated with SUMS.

Inclusion Criteria

Participants were required to have a history of at least one pregnancy.

Exclusion Criteria

Women were excluded if adequate clinical or obstetric information was not available or if they were unable to recall pregnancy-related data reliably.

Convenience sampling was used among eligible clinic attendees. Given the retrospective design and the use of convenience sampling, no a priori sample size calculation was performed; all eligible cases within the study period were included. To collect data, a checklist was developed, which included three sections: a) Demographic Information of Patients at Visit: This section gathered data including age, gender, history of previous illnesses, education level, occupation, economic status, and marital status. b) Information Related to MS at the Time of Visit: This included the type of MS at the time of visit, Expanded Disability Status Scale (EDSS) score, current disease-modifying therapies (DMTs), the timing of MS diagnosis (before or after pregnancy), initiation of MS treatment (before or after pregnancy), DMT exposure before pregnancy, the presence of clinical MS relapses within one year prior to pregnancy, occurrence of clinical MS relapses during pregnancy, and occurrence of clinical MS relapses within three months postpartum. c) Information Related to Pregnancy and Delivery: This section encompassed the number of pregnancies, maternal age at the time of pregnancy and delivery, number of children, number of miscarriages or stillbirths, mode of delivery, infant status and discharge, breastfeeding status, and duration of breastfeeding.

Before completing the questionnaire, patients received thorough information and necessary training from two healthcare professionals at the clinic. Written informed

consent was obtained from all participants or their parents/legal guardians. Also, issues of data confidentiality and anonymity, participant privacy, and participants' right to withdraw from the study without prejudice were upheld. After providing written consent, they completed the questionnaires in a quiet and comfortable environment. During the questionnaire completion, the responsible personnel were present to answer questions and clarify doubts. For illiterate individuals unable to read or write, the two attending officials completed the questionnaires. A separate questionnaire was completed for each delivery. Because some women contributed more than one delivery, analyses were primarily descriptive, and findings should be interpreted with caution regarding statistical independence.

Measured criteria

The primary objective was to descriptively characterize clinical MS relapses occurring within the three months after delivery by mode of delivery (vaginal or cesarean) and, if applicable, type of anesthesia (general, spinal, or epidural). A secondary objective was to descriptively characterize demographic, clinical, obstetric, and treatment-related factors among deliveries with and without postpartum clinical relapse.

Because of the retrospective design, standardized postpartum MRI examinations were not routinely performed. Consequently, the primary outcome was restricted to clinically confirmed relapses, and radiological disease activity was not assessed.

A postpartum relapse was defined as new or worsening neurological symptoms lasting at least 24 hours after a period of clinical stability, in the absence of fever, infection, or other identifiable causes of neurological deterioration (Montalban et al., 2025; Schubert et al., 2023). The treating neurologist confirmed relapse diagnoses through routine clinical assessment and review of clinical records. Because standardized postpartum MRI examinations were not routinely performed, MRI confirmation was not consistently available.

Ethics

This study was performed in line with the principles of the Declaration of Helsinki. Study protocol approval was obtained from the institutional review board and the Ethics Committee of SUMS (IR.SUMS.MED.REC.1403.022).

Statistical Analysis

The data were summarized using descriptive statistics. Descriptive analyses were performed to characterize deliveries with and without postpartum relapse. Continuous variables are presented as mean $\pm$ standard deviation (SD), where appropriate, and categorical variables are reported as frequencies and percentages. Given the very small number of postpartum relapse events and the fact that several women contributed more than one pregnancy, the observations were not fully independent, and potential within-subject correlation was recognized. However, only five postpartum relapse events were observed in the study. Therefore, formal inferential statistical analyses, including multivariable modeling, were not performed. Although correlation-adjusted approaches, such as generalized estimating equations (GEE) or mixed-effects logistic regression, could theoretically account for within-subject clustering, the very limited number of outcome events was considered insufficient to provide stable and reliable estimates using these approaches. Consequently, no p-values, confidence intervals, or effect estimates were calculated. The analyses were therefore restricted to descriptive comparisons, and the findings presented in the Results and Tables should be interpreted as exploratory and hypothesis-generating rather than as formal tests of association. All analyses were conducted using SPSS software version 23.

Results

The final analysis included 83 deliveries from 26 women with MS. These 83 pregnancy episodes were contributed by 26 women over their individual disease courses, with some women contributing multiple pregnancies; therefore, the number of pregnancy episodes should not be interpreted as a population-level fertility estimate. Of these, five deliveries (6%) were followed by a clinical relapse within three months postpartum. Given the limited number of outcome events, the available data were insufficient to support reliable inferential comparisons between delivery groups.

Demographic Characteristics

As shown in Table 1, the mean age of the women at the time of delivery was 29.0 ± 5.16 years overall and was 31.8 ± 5.11 years among deliveries followed by relapse compared with 28.76 ± 5.15 years among those without relapse. The mean number of pregnancies per

TABLE 1: Demographic and Socioeconomic Characteristics of 83 Deliveries in 26 Women with MS

Variables	Total deliveries mean±SD (%) N = 83	With postpartum relapse during 3 months after deliv- ery (N) N= 5	Without postpartum relapse during 3 months after deliv- ery (N) N=78
Age (year)	29.0 ± 5.16	31.80 ± 5.11	28.76 ± 5.15
Number of pregnancies per woman	1.87 ± 0.947	2.40 ± 0.89	1.96 ± 0.94
Duration of MS (year)	7.43 ± 4.243	5.60 ± 4.50	7.55 ± 4.22
EDSS	1.5 ± 1.242	2.80 ± 2.04	1.41 ± 1.14
Level of education			
- Illiterate	10 (12%)	0 (0.0%)	10 (12.8%)
- Undergraduate	11 (13.2%)	0 (0.0%)	11 (14.1%)
- Diploma and associate	35 (42.3%)	2 (40.0%)	33 (42.3%)
- Bachelor's degree or higher	27 (32.5%)	3 (60.0%)	24 (30.8%)
Marital status			
- Single	0	0 (0.0%)	0 (0.0%)
- Married	81 (97.6%)	4(80%)	77(98.7%)
- Divorced	2 (2.4%)	1(20%)	1(1.3%)
Occupation			
- Employed or salaried	19 (22.9%)	2 (40.0%)	17 (21.8%)
- Housekeeper	64 (77.1%)	3 (60.0%)	61 (78.2%)
Socioeconomic state			
- Lower than Normal	32 (38.6%)	1 (20.0%)	31 (39.7%)
- Normal	48 (57.8%)	4 (80.0%)	44 (56.4%)
- Higher than Normal	3 (3.6%)	0 (0.0%)	3 (3.8%)

MS: Multiple Sclerosis, SD: Standard Deviation, N: Number, EDSS: Expanded Disability Status Scale, RRMS: Relapsing-Remitting Multiple Sclerosis, SPMS: Secondary Progressive Multiple Sclerosis, PPMS: Primary Progressive Multiple Sclerosis, PCO: Polycystic Ovary Syndrome, DM: Diabetes Mellitus. Data are presented descriptively as mean ± SD or n (%). No inferential statistical tests were performed because of the small number of postpartum relapse events and repeated deliveries contributed by some participants.

woman was 1.87 ± 0.95 ; some women contributed multiple pregnancy episodes, with each episode recorded according to its pregnancy sequence for that woman. The corresponding mean was 2.40 ± 0.89 in the relapse group and 1.96 ± 0.94 in the non-relapse group.

The mean MS disease duration at the time of delivery was 7.43 ± 4.24 years. The mean disease duration was 5.60 ± 4.50 years among deliveries followed by relapse and 7.55 ± 4.22 years among those without relapse. The mean EDSS score for the overall cohort was 1.5 ± 1.24 . Women with postpartum relapse showed higher mean EDSS scores than those without relapse (2.80 ± 2.04 vs 1.41 ± 1.14).

42.3% of the women held a diploma or associate degree, while 32.5% held a bachelor's degree or higher. Among deliveries followed by postpartum relapse, 60% (n=3) occurred in women with a bachelor's degree or higher, and 40% (n=2) in women with a diploma or associate degree. Almost all women were married (97.6%), and most were housewives (77.1% overall; 60% in the relapse group).

Clinical and Obstetric Features

The most prevalent type of MS was RRMS (91.6%), followed by SPMS (6%) and PPMS (2.4%) (Table 2). Among deliveries followed by postpartum relapse, 60%

occurred in women with RRMS, while 20% each occurred in women with SPMS and PPMS.

Hypothyroidism and PCO were the most common comorbidities, with each affecting 6% of the population. Among deliveries followed by postpartum relapse, hypothyroidism and diabetes mellitus each accounted for 20% of the relapse group, compared with 5.1% and 0%, respectively, among deliveries without relapse.

Before pregnancy, interferon was the most commonly used DMT (54/83 deliveries, 65.1%). Among the five deliveries followed by postpartum relapse, two (40.0%) occurred in women who had been receiving B-cell-depleting therapies before pregnancy, two (40.0%) occurred among those receiving glatiramer acetate, and one (20.0%) occurred among those receiving interferon. Given the small number of postpartum relapse events and the descriptive nature of the analyses, these distributions should not be interpreted as evidence of differences in treatment-related relapse risk.

Two women had received teriflunomide and fingolimod before pregnancy, respectively; however, both treatments were discontinued before conception. The exact interval between treatment discontinuation and conception was not available in the retrospective dataset.

About 20.5% of deliveries had a history of clinical relapse in the year before pregnancy, but a postpartum relapse followed none of these deliveries. Similarly, no postpartum relapse occurred in women who experienced a clinical relapse during pregnancy (6% of the cohort).

Characteristics Related to Delivery

Out of the 83 deliveries, 44.6% (37/83) were vaginal deliveries, comprising 31 normal vaginal deliveries (37.3%), 1 instrument-assisted vaginal delivery (1.2%), 3 water births (3.6%), and 2 vaginal deliveries under spinal anesthesia (2.4%). The remaining 44.6% (37/83) were cesarean sections, including 21 under general anesthesia (25.3%) and 16 under spinal/epidural anesthesia (19.3%). The remaining 9 pregnancies (10.8%) resulted in miscarriage or fetal demise. The distribution of delivery types in the two descriptive groups is presented in Table 2. Of the five postpartum relapse events, two (40%) occurred after normal vaginal delivery and one (20%) after cesarean delivery under general anesthesia. No postpartum relapses were observed among deliveries performed under spinal or epidural anesthesia in this

study.

Two cases (40%) of postpartum relapse transpired in pregnancies ending in miscarriage or fetal demise.

Neonatal and Breastfeeding Outcomes

Most deliveries (84.3%) resulted in mature infants (gestational age ≥ 37 weeks), whereas preterm delivery was infrequent (4.8%). No postpartum relapse was observed among the four deliveries involving preterm birth (0/4); however, given the very small number of preterm deliveries and relapse events, these descriptive findings do not permit conclusions regarding a potential relationship between preterm birth and postpartum relapse. Of the five postpartum relapse events, three (60%) occurred following delivery of an infant born at ≥ 37 weeks' gestation, while two (40%) occurred after pregnancies that ended in abortion or fetal demise.

Overall, breastfeeding was reported for 56 of 83 pregnancy episodes (67.5%). Breastfeeding was reported in 2 of 5 deliveries, followed by postpartum relapse (40.0%), and 54 of 78 deliveries without relapse (69.2%). Among breastfeeding deliveries, breastfeeding duration was ≤ 7 months in 19/56 (33.9%), 7–12 months in 9/56 (16.1%), and ≥ 12 months in 28/56 (50.0%). Among the two relapse events occurring after breastfeeding deliveries, none occurred in the ≤ 7 -month category, while one (50.0%) occurred in the 7–12-month category and one (50.0%) in the ≥ 12 -month category. Given the very small number of postpartum relapse events, these descriptive distributions should be interpreted cautiously and do not permit conclusions regarding a relationship between breastfeeding duration and postpartum relapse.

Discussion

The current study descriptively characterized postpartum clinical relapse according to mode of delivery during the initial three months after childbirth and described additional demographic and clinical characteristics of deliveries with and without relapse. Among female patients with MS, 26 had experienced pregnancy after MS diagnosis (83 deliveries). A considerable proportion of women with MS choose not to pursue pregnancy after diagnosis, likely due to a combination of disease-related, psychosocial, and healthcare system factors. Studies show that only between 20% and 33% of women with MS have experienced pregnancy after the diagnosis (van der Kop et al., 2011). This decision is

TABLE 2: Obstetric and Clinical Characteristics of 83 Deliveries in 26 Women with MS

Variables	Total deliveries (N%) N = 83	With postpartum re- lapse during 3 months after delivery (N%) N= 5	Without postpartum relapse during 3 months after delivery (N%) N=78
MS phenotype			
RRMS	76(91.6%)	3(60.0%)	73(93.6%)
SPMS	5(6%)	1(20.0%)	4(5.1%)
PPMS	2(2.4%)	1(20.0%)	1(1.3%)
Past medical history			
Hypothyroidism	5(6%)	1(20.0%)	4(5.1%)
PCO	5(6%)	0(0%)	5(6.4%)
DM	1(1.2%)	1(20%)	0(0%)
Psoriasis	1(1.2%)	0(0%)	1(1.3%)
Others	4(4.8%)	0(0%)	4(5.1%)
No PMH	67(80.7%)	3(60.0%)	64(82.1%)
Pre-pregnancy DMT exposure			
Not yet	3(3.6%)	0(0%)	3(3.8%)
B cell therapy	8(9.6%)	2(40%)	6(7.7%)
Dimethyl fumarate	9(10.8%)	0(0%)	9(11.5%)
Interferon	54(65.1%)	1(20%)	53(67.9%)
Fingolimod	1(1.2%)	0(0%)	1(1.3%)
Teriflunomide	1(1.2%)	0(0%)	1(1.3%)
Glatiramer acetate	7(8.4%)	2(40.0%)	5(6.4%)
History of relapse in the year before pregnancy			
Yes	17(20.5%)	0(0%)	17(21.8%)
No	66(79.5%)	5(100%)	61(78.2%)
Relapse occurrence during pregnancy			
Yes	5(6.0%)	0(0.0%)	5(6.4%)
No	78(94.0%)	5(100.0%)	73(93.6%)
Route of delivery			
NVD	31(37.3%)	2(40%)	29(37.2%)
Instrument-assisted vaginal delivery	1(1.2%)	0(0%)	1(1.3%)
Water	3(3.6%)	0(0%)	3(3.8%)
Spinal	2(2.4%)	0(0%)	2(2.6%)
C/S with general anesthesia	21(25.3%)	1(20.0%)	20(25.6%)
C/S with spinal/epidural anesthesia	16(19.3%)	0(0%)	16(20.5%)
Abortion and Dead fetus	9(10.8%)	2(40.0%)	7(9.0%)
Newborn condition			
Premature: Gestational age <37 weeks	4(4.8%)	0(0%)	4(5.1%)
Mature: Gestational age ≥37 weeks	70(84.3%)	3(60.0%)	67(85.9%)
Abortion and Dead fetus	9(10.8%)	2(40.0%)	7(9.0%)
Breast-feeding			
Yes	56(67.5%)	2(40%)	54(69.2%)
No	18(21.7%)	1(20%)	17(21.8%)
Abortion and Dead fetus	(10.8%)9	(40%)2	(9%)7

Continuation of Table 2:

Duration of breastfeeding (months), among breastfeeding deliveries			
≤7	19/56(33.9%)	0/2(0%)	19/54(35.2%)
7-12	9/56(16.1%)	1/2(50%)	8/54(14.8%)
≥12	28/56(50%)	1/2(50%)	27/54(50%)

DMT: Disease-Modifying Therapy, NVD: Normal Vaginal Delivery, C/S: Cesarean Section N: Number. Data are presented descriptively as N (%). No inferential statistical tests were performed because of the small number of postpartum relapse events and repeated deliveries contributed by some participants

influenced by concerns about disease course and treatment safety, MS-related physical and cognitive limitations, psychological burden, and limited access to specialized perinatal MS care.

With scientific advances, attitudes toward pregnancy in women with MS have shifted to a more positive view, and some studies have shown that pregnancy can temporarily reduce MS relapses. This effect is greater during pregnancy, and after delivery, the likelihood of relapses increases, especially in the first three to four months after delivery and in women with active MS before pregnancy. These immunological changes are thought to reflect a shift toward a more anti-inflammatory state during pregnancy, followed by reactivation of immune pathways in the early postpartum period (Confavreux et al., 1998).

In line with the primary objective of the study, postpartum relapse events were observed across several delivery categories. However, given the small number of relapse events and the absence of inferential statistical testing, the present findings do not permit conclusions regarding an association between mode of delivery and postpartum relapse. Nevertheless, the descriptive pattern observed in our cohort is broadly consistent with previous studies suggesting that obstetric decisions in women with MS should generally not be modified solely because of maternal MS (Bouvet et al., 2021). Previous cohort studies have also reported no significant impact of delivery mode or type of anesthesia on postpartum MS activity. For example, Harazim et al. (2018), in a retrospective cohort study with six-month postpartum follow-up, reported no association between obstetric anesthesia/analgesia and disease course (Harazim et al., 2018). Similarly, Pastò et al. (2012) reported that epidural analgesia was not associated with an increased risk of postpartum relapse (Pastò et al., 2012).

Taken together, these findings and the descriptive ob-

servations from our cohort show that postpartum relapse events occurred across several delivery categories, but do not permit conclusions regarding differences in relapse occurrence between these categories. However, the very small number of postpartum relapse events ($n = 5$) substantially limits this study's ability to detect potentially meaningful differences between delivery categories. Although no formal statistical power or hypothesis-testing analysis was performed, the sparse number of outcome events and repeated pregnancies reported by some women substantially constrain the precision and interpretability of the observed descriptive patterns. Therefore, these findings should be regarded as preliminary, exploratory, and hypothesis-generating rather than as evidence for or against an association between delivery mode and postpartum relapse. Larger prospective studies with adequate numbers of relapse events and appropriate correlation-adjusted statistical methods are needed to more reliably evaluate the relationship between delivery mode, anesthesia, and postpartum disease activity.

The observed postpartum relapse rate (6%) was lower than that reported in historical cohorts such as the PRIMS study (Confavreux et al., 1998). The lower observed relapse frequency may reflect differences in preconception counseling, treatment strategies, patient characteristics, or other aspects of clinical management; however, these explanations could not be evaluated in the present descriptive study. Evidence suggests that preconception disease stability and coordinated treatment planning markedly diminish postpartum activity (Vukusic et al., 2004).

It should be noted that postpartum disease activity was assessed exclusively based on clinically recognized relapses. MRI is reported to be the most sensitive tool for monitoring disease activity in MS, and clinical activity alone does not fully reflect the overall disease burden

(Dobson and Giovannoni 2019). However, MRI was not systematically performed during the postpartum period because of the retrospective design. Therefore, subclinical inflammatory activity, including new or enlarging T2 lesions and gadolinium-enhancing lesions, may have remained undetected. Consequently, the observed relapse rate likely underestimates the total burden of postpartum disease activity.

While postpartum relapse events were observed across several delivery categories, various patient-related characteristics showed different descriptive distributions between deliveries with and without relapse. Women who experienced relapses had higher baseline disability, aligning with studies indicating that baseline disability scores correlate with structural and inflammatory markers in MS—including lesion volume and brain atrophy—and thus reflect long-term inflammatory and neurodegenerative disease activity (Marciniewicz et al., 2019). Moreover, hypothyroidism and diabetes mellitus were observed more frequently among deliveries followed by relapse, although the small number of events precludes interpretation of these distributions as evidence of an association. Autoimmune thyroid disease has been consistently associated with MS and may contribute to systemic immune dysregulation (Gautam et al., 2023). Likewise, diabetes mellitus may intensify inflammatory responses and oxidative stress, worsening CNS susceptibility (Association 2018). In addition, recent studies have shown that a burden of comorbidity, particularly metabolic diseases such as diabetes, is associated with increased MS disease activity—including higher relapse rates (Marrie et al., 2023; Salter et al., 2024).

Regarding pre-pregnancy DMT exposure, two of the five deliveries followed by postpartum relapse (40.0%) occurred in women who had received B-cell-depleting therapies before pregnancy, two (40.0%) in women who had received glatiramer acetate, and one (20.0%) in a woman who had received interferon. However, given the very small number of postpartum relapse events and the absence of inferential statistical analyses, these descriptive differences should not be interpreted as evidence that any specific DMT increases or decreases the risk of postpartum relapse. Recent studies have shown that the type, timing, and discontinuation or reinitiation of DMTs may influence disease activity during pregnancy and the postpartum period (Bast et al., 2025; Yeh et al.,

2024). In particular, women treated with high-efficacy therapies such as anti-CD20 agents may have different postpartum relapse patterns; however, treatment selection in clinical practice is strongly influenced by underlying disease activity and severity (Sahloul et al., 2024). Therefore, the distribution of postpartum relapses across DMT categories in the present cohort may reflect confounding by indication and other treatment-related factors rather than a direct effect of the DMT itself. This potential confounding could not be adequately addressed in the present study because of the limited number of relapse events and the absence of multivariable analyses. Larger prospective studies with detailed information on pre-pregnancy disease activity, DMT exposure, timing of treatment discontinuation, and postpartum treatment reinitiation are needed to clarify the relationship between DMT use and postpartum relapse risk.

Another important consideration is the timing of DMT discontinuation before conception and reinitiation after delivery, as both may influence postpartum disease activity (Bast et al., 2025; Yeh et al., 2024). These variables were not consistently available in our retrospective dataset and, therefore, could not be evaluated. Consequently, their potential confounding effects cannot be excluded.

No postpartum relapse was observed among women with a history of relapse before or during pregnancy in this study. This finding contrasts with the classic PRIMS reports that identified pre-pregnancy and pregnancy relapse as predictors of postpartum relapse (Vukusic et al., 2004). This discrepancy may reflect changes in clinical management and preconception counseling. Recent studies and reviews suggest that the type and timing of DMTs, including the use or delay of anti-CD20 therapies, as well as the regular scheduling and timely reinitiation of DMTs postpartum, can reduce relapse risk (Yeh et al., 2024). Therefore, expert counseling and therapy optimization in our cohort may have reduced postpartum clinical relapse activity. In addition, recent reviews and evidence-based recommendations emphasize the importance of multidisciplinary pregnancy planning and risk-based preconception management to improve maternal outcomes (Melo et al., 2024). Therefore, the observed differences between our findings and previous studies may be due to changes in treatment and counseling strategies rather than to discrepancies in the disease's biological model.

In the present study, breastfeeding was reported for

40.0% of deliveries, followed by postpartum relapse, and for 69.2% of deliveries without postpartum relapse. Our descriptive findings did not establish a protective effect, given the small number of postpartum relapse events. However, the role of breastfeeding, particularly exclusive breastfeeding, has been highlighted as a potential protective factor against the recurrence of disease relapses. Some research focusing on exclusive breastfeeding has shown that this practice may be associated with a reduced rate of postpartum relapses. In particular, the study by Langer-Gould et al. (2009) was the first to differentiate between exclusive and non-exclusive breastfeeding, finding that relapse rates were significantly higher in women who did not exclusively breastfeed, regardless of their disease history or pre-pregnancy treatments (Langer-Gould et al., 2009). Breastfeeding has been proposed as a potential protective factor against postpartum relapse, particularly when exclusive, although evidence remains inconsistent across studies. The proposed association may be mediated by hormonal changes associated with lactational amenorrhea and immune modulation during exclusive breastfeeding. Meta-analyses also support this view. For example, Krisko et al. (2019) demonstrated in a meta-analysis that women with MS who breastfed postpartum, particularly exclusively, had a 37% lower chance of experiencing a relapse (Krisko et al., 2020).

However, it should be noted that study results are heterogeneous due to differences in study designs, follow-up durations, and definitions of breastfeeding. Overall, the available evidence suggests that breastfeeding, particularly exclusive breastfeeding, may play a protective role against the recurrence of MS after childbirth and could be part of postpartum management strategies for women with this condition. Our descriptive findings do not independently establish this protective effect.

These findings suggest that obstetric considerations, rather than neurological status alone, may play a more prominent role in delivery planning for women with MS, in line with current international recommendations. Instead, pre-existing comorbidities, level of disability, and pre-pregnancy DMT exposure showed notable descriptive distributions among deliveries followed by relapse and may warrant further evaluation in adequately powered studies. These factors should be carefully considered when planning for pregnancy and after giving birth. Given the limited number of relapse events and

the repeated pregnancies reported by some participants, our findings should be interpreted primarily as descriptive observations that require confirmation in larger prospective cohorts using correlation-adjusted statistical approaches.

Limitations

There are several limitations to this study. First, its retrospective design increases the likelihood of recall bias and incomplete records, especially regarding the timing of relapses and symptom severity. Although MS relapses and childbirth are generally memorable events, reliance on patient self-report may still have affected data accuracy. Although women unable to reliably recall pregnancy-related information were excluded, the interval between delivery and data collection varied among participants and was not systematically recorded. Therefore, recall bias regarding obstetric history and the timing of postpartum relapses cannot be completely excluded. Second, the number of women who experienced pregnancy after MS diagnosis was relatively small (26 women, 83 deliveries), limiting statistical power and generalizability. In addition, repeated deliveries from the same women resulted in non-independent observations and potential within-subject correlation. Although correlation-adjusted statistical models could theoretically account for this clustering, the very small number of postpartum relapse events ($n = 5$) precluded reliable estimation using such approaches. Therefore, the analyses were limited to descriptive comparisons, and residual clustering-related bias cannot be excluded. The third limitation is the absence of standardized postpartum MRI surveillance. Because radiological disease activity often exceeds clinically apparent relapse activity, reliance on clinical relapse alone may have underestimated inflammatory disease activity in this cohort. Therefore, the present findings should be interpreted as reflecting clinical rather than overall disease activity. Furthermore, variability in DMT exposure, particularly regarding the timing of treatment cessation before conception, may result in confounding effects that could not be fully controlled. Detailed information regarding the timing of DMT discontinuation before conception and postpartum treatment re-initiation was unavailable, preventing evaluation of these important clinical determinants of postpartum relapse. This limitation is particularly relevant for therapies such as fingolimod,

for which disease reactivation after treatment discontinuation during pregnancy has been reported. Moreover, treatment-related analyses were subject to confounding by indication, because women receiving different DMTs differed in their baseline disease characteristics, which could not be adjusted for in the present study. Lastly, another important limitation is the very small number of postpartum relapse events. Although this reflects the relatively low relapse frequency in the study population, it substantially reduced the statistical power to detect potential differences between delivery groups. Consequently, the possibility of a type II error cannot be excluded.

Conclusion

In conclusion, this retrospective cohort study provided descriptive information on postpartum clinical relapse across different delivery categories. However, the small number of relapse events and the absence of inferential statistical testing preclude concluding an association between delivery mode and postpartum relapse. These findings should be interpreted with caution and warrant further evaluation in larger prospective studies. The descriptive findings do not support changing obstetric decision-making solely based on concern about postpartum MS relapse; however, delivery decisions should continue to be individualized according to standard obstetric and neurological considerations. Several patient-related characteristics, including comorbidities, baseline disability, and pre-pregnancy DMT exposure, showed different descriptive patterns among deliveries followed by relapse and warrant further investigation. The relatively low observed relapse rate may reflect improved preconception counseling, disease control, and coordinated peripartum care, although these factors were not formally evaluated in the present study. Additional prospective studies with larger sample sizes and systematic MRI monitoring are necessary to elucidate predictors of postpartum clinical relapse activity and to enhance clinical guidelines for pregnancy management in women with MS.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was obtained from the Institutional Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1403.022).

Data availability statements

The data are available from the corresponding author on reasonable request.

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