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Pregnancy before and after NMOSD diagnosis: a retrospective study highlighting the challenges in a referral center in Brazil

Elisa Matias Vieira de Melo[1], Rafael Chaves Claudino de Queiroga[1], Eliana Tomomi Shimabukuro[1] and Maria Fernanda Mendes[1]

Abstract

Introduction: Addressing pregnancy-related management issues and the use of medications during this period is crucial in routine clinical consultations for women of childbearing age with neuromyelitis optica spectrum disorder (NMOSD).
Objective: To evaluate the epidemiological and clinical characteristics of patients with NMOSD who reported pregnancy, as well as pregnancy outcomes and neonatal data.
Methods: We included patients seen between January 2024 and July 2025. Data were gathered through medical record reviews and targeted interviews, focusing on pregnancy, postpartum, and childbirth outcomes.
Results: Among the patients included, a total of 52 pregnancies were reported, of which 15 occurred after the diagnosis of NMOSD. No statistically significant differences were observed in variables such as maternal age at pregnancy, pregnancy complications, relapses during and after pregnancy, birth weight, or birth length. However, there was a trend towards older maternal age at pregnancy in patients diagnosed with NMOSD.
Conclusion: The impact of NMOSD on pregnancy should be carefully considered during family planning. This approach is essential for effective contraception or the planning of a well-supported pregnancy under the guidance of a multidisciplinary team.

Keywords

Family planning, pregnancy, neuromyelitis optica

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Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a rare condition, with a prevalence ranging from 0.5 to 4 per 100,000. It is more common in women, with an average onset around the age of 40, which often coincides with childbearing age.[1,2]

During pregnancy, fluctuations in estrogen and progesterone levels shift the immune response from Th1 to Th2, which, given the pathophysiology of NMOSD, may negatively impact disease activity. Additionally, the well-known AQP4 antibody, implicated in the disease's pathophysiology, is expressed in human placental syncytiotrophoblasts, so NMO-IgG binds the placental syncytiotrophoblast of fetal villi and activates the classical complement pathway, potentially leading to unfavorable outcomes.[3] Recent studies have indicated an increased annualized relapse rate (ARR) after 3 months postpartum, though no significant impact was observed during pregnancy.[4] Furthermore, there is evidence of higher miscarriage rates.[5] Consequently, functional decline has been reported during pregnancy and after childbirth.

Additionally, some of the current treatments for NMOSD are known to carry risks for the developing fetus, and safety data for others remain limited.[6]

[1]Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo/SP, Brazil

Corresponding author:
Elisa Matias Vieira de Melo, Faculdade de Ciências Médicas da Santa Casa de São Paulo, Avenida Onze de Junho, 1070, Sala 510. Vila Clementino, São Paulo/SP, Brazil.
Email: elisa.melo@fcmsantacasasp.edu.br

With the increasing availability of treatment options for NMOSD, it is essential to recognize the unmet needs of this chronic and incurable disease, with family planning being one of the central themes. In this context, discussing the characteristics of pregnancy in these patients and the use of medications during this period will be crucial points in routine consultations.

Methods

A study conducted at the Demyelinating Diseases of the Central Nervous System clinic at Santa Casa de São Paulo included patients between January 2024 and July 2025 who met the revised 2015 Wingerchuk criteria for NMOSD. Data were collected from medical records and targeted interviews to gather information on pregnancy, postpartum, and childbirth. Inclusion criteria were female sex, age over 18 years, diagnosis of NMOSD according to valid criteria.[1] Exclusion criteria were non-consent to participate, patients we weren't able to contact, and disease onset age above 45 years.

All patients who met the inclusion criteria were interviewed to collect epidemiological data, clinical information, and pregnancy history.

The data for this retrospective study were obtained from our NMOSD database, including demographic data, age at onset, disease duration, history of attacks, ARR (the number of attacks per patient-year), Expanded Disability Status Scale (EDSS), AQP4-Ab serostatus (cell-based assay, CBA), and therapeutic regimen. Additionally, during patient interviews, information on obstetric data was collected, including the number of pregnancies, fetal outcomes of each pregnancy, and methods of delivery. We considered the data for all pregnancies reported by the patients, whether they occurred before or after the onset of the disease.

The data were tabulated into an Excel spreadsheet and then exported to SPSS version 25.0. In the Descriptive Analysis, absolute (n) and relative (%) frequencies were calculated for qualitative variables, while summary measures (mean, standard deviation, median, range (minimum and maximum)) and boxplots were used for quantitative variables. In the Inferential Analysis (statistical tests), the following tests were applied: Fisher's exact test for qualitative variables, Shapiro–Wilk test for normality, and Student's t-test for comparing quantitative variables by pregnancy stage. A significance level of 5% was adopted for all statistical tests.

Results

We collected data from 43 female patients with a diagnosis of NMOSD, of which data from 52 pregnancies were analyzed after applying the inclusion or exclusion criteria. Of these, 37 occurred before NMOSD diagnosis, 15 after diagnosis, and none during pregnancy.

Table 1. Descriptive characteristics ($n = 43$).

		% (N)
Age, years	Average: 39.6 (19 −70)	
Ethnicity	White	48.8 (21)
	Hispanic	41.9 (18)
	Black	9.3 (4)
Schooling	0–8 years	9.3 (4)
	9–12 years	51.2 (22)
	>12 years	39.5 (17)
Occupation	Medical license/retired	32.6 (14)
	Formal employed	23.3 (10)
	Unformal employed	13.9 (6)
	Unemployed	20.9 (9)
	Other (e.g., student, homemaker)	9.3 (4)
EDSS	Average: 3.5 ($N = 32$)	

Table 2. Current and previous treatment ($n = 43$).

Treatment, n (%)	Current	Previous
Azathioprine	17 (39.35)	14 (32.5)
Mycophenolate mofetil	4 (9.3)	4 (9.3)
Rituximab	14 (32.6)	12 (27.6)
Tocilizumab	2.3 (1)	0
Inebilizumab	2.3 (1)	0
Satralizumab	2.3 (1)	0
Others	2 (4.7)	3 (7)
No treatment	3 (7)	10 (23.3)

Demographic data are described in Table 1. Regarding employment status, 58.4% are unemployed or receiving government benefits.

Among the 43 patients included, 74.4% ($n = 32$) were positive for aquaporin-4 antibodies, 18.6% ($n = 8$) were seronegative, and serological status was unknown in 7.0% ($n = 3$). Considering the treatment history, Azathioprine is the most prevalent current and previous medication (Table 2).

Regarding obstetric and neonatal outcomes, caesarean delivery occurred in 29 of 52 births. No statistically significant differences were observed in the evaluated variables when comparing pregnancies occurring before versus after NMOSD diagnosis (maternal age at pregnancy, pregnancy complications, relapses during and after pregnancy, birth weight, and birth length). The mean birth weight was 3130 grams ($n = 45$; range 1000–4300 g), and 7 of 52 deliveries were preterm. No cases of perinatal mortality were observed in this cohort. Data on neonatal intensive care unit or intermediate care unit admissions were not consistently available in the medical records and could therefore not be analyzed. Considering the history of pregnancy-related complications, a total of 14 pregnancy-related adverse events were documented, including premature rupture of membranes ($n = 2$), first-trimester vaginal bleeding ($n = 2$), preeclampsia ($n = 2$), perinatal depression ($n = 3$), placental abruption ($n = 3$), and gestational diabetes ($n = 2$). Among patients with adverse

events, chronic hypertension was identified as a relevant confounding factor in one case; no other major confounders, such as pre-existing diabetes or substance abuse, were identified in the available medical records.

A trend toward older maternal age at pregnancy was observed among women who became pregnant after NMOSD diagnosis compared with those whose pregnancies occurred before diagnosis.

Regarding treatment during pregnancy, azathioprine was continued in two patients, while it was discontinued at the beginning of pregnancy in two others. No other immunosuppressive therapies were used during pregnancy.

During the postpartum period (first 12 months), among the patients already diagnosed with NMOSD, 7 experienced relapses, with 2 of them being on azathioprine. About breastfeeding, 13 were able to breastfeed, while the other 2 faced difficulties resuming breastfeeding after receiving treatment for the relapses, which occurred within the first month after delivery.

Discussion

In our country, the majority of patients are of mixed-race or Black ethnicity and come from low-income households, which results in difficulty accessing high-complexity medical services, something that the diagnosis and treatment of NMOSD require.[7,8] Despite our patient sample being composed mostly of White individuals with a good level of education (the majority having more than 8 years of schooling), most of them are unemployed or receiving government assistance, which increases their social vulnerability.

Azathioprine was the most commonly used medication, both as current and previous therapy, that can be explained by limited access to treatments and lower socioeconomic conditions. Access to Rituximab (RTX) in our country is hindered by the lack of governmental protocols for its use, despite the broad scientific evidence supporting this medication in disease control, even though it is off-label. Therefore, patients start RTX but are unable to continue treatment and must return to oral immunosuppressants like azathioprine and mycophenolate mofetil. Moreover, these are generally low-income patients, which complicates their access to and maintenance in a consistent care pathway.[9,10] In our country, there is no public access to medications approved for the treatment of NMOSD. Access through the private healthcare sector, for patients covered by health insurance, is limited and often challenging, with the majority of cases requiring legal action to obtain treatment.

In our study, we did not identify any differences in pregnancy variables between the group that became pregnant before and the group that became pregnant after the diagnosis. From our literature review on the subject, it is often mentioned that, unlike multiple sclerosis, a reduction in disease activity does not occur in NMOSD.[11,12] In the theoretical model, pregnancy-induced changes in immune tolerance, which increase Th2-mediated immune responses and stimulate humoral immunity, could potentially exacerbate autoantibody-mediated diseases during pregnancy. However, studies found that pregnancy-related attacks were most common after delivery.[4,13] This discrepancy between theoretical expectations and clinical observations is not well understood. Therefore, it is plausible that other underlying pathophysiological mechanisms responsible for NMOSD activity after pregnancy may be involved.[14,15]

It is interesting to note the tendency towards later pregnancies (above 30 years old) in patients who had already been diagnosed, which can be explained by the impact of the diagnosis on the family planning of these patients. Factors delaying pregnancy plans include post-relapse recovery, initiation and adjustment of therapy, and concerns about pregnancy after diagnosis.

Another important consideration is the continuation of therapies during pregnancy. Studies indicate that proper treatment during pregnancy is directly correlated with controlling disease activity in the postpartum period.[16,6] In our cohort, azathioprine was discontinued in two patients following the recommendation of their obstetricians. Azathioprine can be maintained during pregnancy, although there are no specific data on NMOSD patients, but, given the experience from other specialties and considering the risks of disease relapse if the medication is discontinued during pregnancy, it is important to continue its use.[17–19] Ideally, family planning should include discussion of treatment strategies such as rituximab prior to conception, aiming for disease control before pregnancy.[20] Monoclonal antibodies approved for the treatment of NMOSD have emerging safety data in the context of pregnancy and breastfeeding.[21] Case reports involving satralizumab have shown no adverse neonatal outcomes, with undetectable levels of the drug in cord blood, infant serum, and breast milk.[22,23] Eculizumab and Ravulizumab, although primarily studied in patients with paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome, have demonstrated favorable maternal and fetal outcomes, including high rates of live births and no increase in congenital anomalies.[21]

Considering the significant increase in relapse rate during the first 3 months postpartum compared to the pre-pregnancy rate, it is important to evaluate and maintain the use of medications in the postpartum period. However, the woman's desire to breastfeed should also be considered. In this regard, there is evidence, once again from studies on diseases other than neurological ones, supporting the use of immunosuppressants and monoclonal antibodies during breastfeeding. Azathioprine is not recommended during breastfeeding in prescribing information, but studies in patients with lupus, chronic intestinal inflammatory diseases, and transplants have found very low or undetectable concentrations in human milk.[24] Additionally, Mahadevan et al.[24] found no adverse effects in the follow-up of children exposed to

azathioprine during breastfeeding. Rituximab also shows low concentrations in breast milk, and no serious adverse effects, such as hematological alterations, have been reported.[25,26] Further data are required to establish the safety of eculizumab, inebilizumab, ravulizumab, and satralizumab during pregnancy and breastfeeding.[21]

Due to the potential impact of NMOSD on pregnancy, previous studies have classified NMOSD pregnancies as high risk, with an increased incidence of maternal and obstetric complications. Reported findings include a higher rate of miscarriage (43%) after disease onset compared to 7% prior to diagnosis within the same population, as well as an increased prevalence of preeclampsia and eclampsia (12%) among AQP4-IgG seropositive women, compared to 3% in the general population.[5,11,20] In our study, no statistically significant differences were observed in maternal or neonatal outcomes when comparing pregnancies before and after NMOSD diagnosis. However, we documented 14 pregnancy-related complications, including cases of preeclampsia and placental abruption, which raise concern and warrant close monitoring.[21]

Beyond individual clinical factors, our findings highlight systemic challenges that directly affect pregnancy outcomes in women with NMOSD. The lack of a structured multidisciplinary care model integrating neurology, maternal–fetal medicine, and obstetric services results in fragmented decision-making, delayed therapeutic adjustments, and inconsistent counseling on pregnancy and breastfeeding. Furthermore, the absence of an organized maternal medicine network limits access to preconception counseling, timely referral to specialized care, and evidence-based management during pregnancy and the postpartum period. These shortcomings are compounded by administrative and judicial barriers to effective immunotherapies, frequently leading to treatment interruption or suboptimal disease control. Together, these structural limitations constitute healthcare-related harm, increasing maternal comorbidity, relapse risk, and long-term neurological sequelae, with potential repercussions for obstetric and neonatal health.

As a limitation, we conducted a retrospective study, which may lead to recall bias when asking for pregnancy-related data from these patients, although such information is typically well remembered by mothers. Our sample was small, limiting statistical analysis.

Conclusion

Given the growing understanding of the pathophysiology of NMOSD and the constantly evolving therapeutic arsenal, it is crucial to understand and characterize the female population affected by the disease to better organize reproductive healthcare for these women. The assessment of the disease's impact on the course of pregnancy, as well as the variables involved in this process, such as the use of disease-modifying drugs/immunosuppressants, social support, disease activity, and disabilities should be evaluated in family planning.

Optimizing care depends on proactive preconception counseling, individualized therapeutic planning, and careful monitoring throughout pregnancy and after delivery, particularly given the increased risk of relapse in the postpartum period. The appropriate selection and continuation of immunosuppressive or immunomodulatory therapies compatible with pregnancy and breastfeeding are essential to minimize disease-related morbidity. A coordinated multidisciplinary approach involving neurology, maternal–fetal medicine, and obstetric care, together with timely access to effective treatments, is crucial to reduce fragmented care, prevent avoidable harm, and support informed reproductive decision-making in women living with NMOSD.

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ORCID iD

Elisa Matias Vieira de Melo https://orcid.org/0000-0001-6448-8277

Ethical approval

The study protocol was approved by Santa Casa de São Paulo's Institutional Review Board (number 76946723.1.0000.5479).

Informed consent

Informed consent was used, and only respondents agreeing to its terms were allowed to continue participating in the survey.

Contributorship

EMVM: conceptualization, investigation, data curation, formal analysis, writing—original draft, writing—review & editing. RCCQ: data curation, writing—review & editing. ETS: writing—review & editing. MFM: formal analysis, writing—review & editing.

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Guarantor

EMVM is the guarantor of the study.

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