

# Multiple sclerosis and infertility: is there any relationship?

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### Introduction

With the introduction of Disease-Modifying Therapies (DMTs), patients affected by Multiple Sclerosis (MS) no longer have to abandon their reproductive plans. However, the relationship between MS and infertility remains unclear. It is still uncertain whether the prevalence of infertility in MS patients is comparable to that of the general population or if it is higher [1]. Several factors may confound the relationship between MS and infertility, including ongoing treatments (some of which are teratogenic), disease progression, and patients' concerns about pregnancy. While limited studies suggest no significant difference in infertility prevalence between MS patients and the general population [2], available data are scarce and often conflicting. Time To Pregnancy (TTP) is a key measure of fecundity and is particularly relevant for MS patients, who may have a narrow window for conception due to treatment intervals.

## **Objectives**

This study aims to evaluate the time to pregnancy in couples where at least one partner has MS, the incidence of infertility, pregnancy rates achieved through Assisted Reproductive Technologies (ART), and pregnancy outcomes in terms of live births. In 2011, we established a multidisciplinary protocol in collaboration with the Multiple Sclerosis Unit. All patients (both male and female) planning to conceive were offered a consultation with a reproductive specialist to assess fertility status and address any subfertility factors. Couples in which one partner had MS were prospectively followed from referral by neurologists until conception and delivery. Collected data included baseline patient characteristics (age, Anti-Müllerian Hormone [AMH] levels, semen parameters, ultrasound findings), time to pregnancy, conception method (spontaneous or ART), and pregnancy outcomes.

## **Results**

A total of 71 couples underwent preconceptional assessment before attempting pregnancy. The affected partner was female in most cases, with only two couples having a male partner with MS. A 12-month follow- up was completed for 57 couples; 11 couples (15.4%) were lost to follow-up, one couple postponed pregnancy due to an MS relapse, and two couples were still within their first year of attempts. Among the 57 couples with at least 12 months of follow-up, 33 achieved at least one spontaneous pregnancy (57.9%), resulting in a total of 45 spontaneous pregnancies. The mean TTP was 5.3 months (±6.2). The remaining 24 couples (42.1%) did not achieve a spontaneous pregnancy within 12 months and were classified as infertile. Among them, 20 opted for ART treatment, with 7 achieving pregnancy (35%), while four couples were still undergoing ART at the time of analysis. Four couples conceived spontaneously after more than 12 months of attempts. The mean age at conception was 32.9 years (±4.6) for those who conceived spontaneously and 36.7 years (±5.8) for those who conceived through ART. Among the 45 spontaneous pregnancies, 35 resulted in the birth of healthy full-term infants (77.7%), nine ended in first-trimester miscarriage, and one was terminated due to worsening neurological condition. Among the 7 pregnancies achieved via ART, five resulted in healthy full-term births (71.4%), while one ended in miscarriage and one in ectopic pregnancy. Regarding ongoing DMT use, therapy was continued in 31.1% of spontaneous pregnancies and 14.3% of ART pregnancies, mostly with Natalizumab.

## **Conclusions**

This prospective observational study highlights a relatively high percentage of MS-affected couples who do not conceive spontaneously within 12 months of unprotected intercourse. However, due to the limited sample size, we cannot conclude with certainty that infertility rates are higher in this population compared to the general population, particularly as maternal age was a major factor influencing TTP. Additionally, the increasing use of Natalizumab in young MS patients may reduce the need for pregnancy delays related to DMT washout, which was one of the main reason to postpone pregnancy in the last decades. These findings bring attention to the importance of implementing multidisciplinary protocols to assess fertility in MS patients early in their reproductive planning. Timely evaluation and, when necessary, access to ART may help reduce time to pregnancy while minimizing disease-related complications.

# **Bibliography**

1 Massarotti C, Inglese M, Anserini P. Fertility in multiple sclerosis patients: still many unanswered questions. Reprod Biomed Online. 2020;41(3):567. 2 Thöne J, Kollar S, Nousome D, et al. Serum anti-Müllerian hormone levels in reproductive-age women with relapsing-remitting multiple sclerosis. Mult Scler. 2015;21(1):41-7.