

Preconception counseling impact in pregnancy outcomes in patients with spondylarthritis

Beirão T¹, Nicolau R^{2,5}, Santos I², Guimarães F³, Aguiar F^{4,5}, Ganhão S^{4,5}, Rodrigues M^{4,5}, Filipa N², Rocha A⁶, Monteiro S⁶, Videira T¹, Brito I^{4,5}

¹ Rheumatology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, Porto, Portugal

² Rheumatology Department, Centro Hospitalar Tondela-Viseu, Viseu, Portugal

³ Pediatric Department, Centro Hospitalar Entre Douro e Vouga, Santa Maria da Feira, Portugal

⁴ Pediatric and young adult Rheumatology unit, Centro Hospitalar Universitário de São João, Porto, Portugal

⁵ Faculty of Medicine, University of Porto, Porto, Portugal

⁶ Obstetrics Department, Centro Hospitalar Universitário de São João, Porto Portugal

Correspondence to

Tiago Beirão

E-mail: tiagobeirao11@gmail.com

Submitted: 11/10/2023

Accepted: 21/01/2024

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article'

© 2024 Portuguese Society of Rheumatology

This article is protected by copyright. All rights reserved.

Abstract

Introduction: Spondylarthritis (SpA) is a group of chronic inflammatory diseases, often affecting women in reproductive age, which can have a significant impact on the reproductive health of women. Preconception counselling and medication adjustments have shown to reduce flares and improve pregnancy outcomes in women with rheumatoid arthritis. However, in women with SpA, data of the impact of preconception counselling on pregnancy outcomes is scarce. The aim of this study is to evaluate its impact.

Methods: In this retrospective multicentric study, data was collected from medical records of women who gave birth from 2020 to 2022. The study included 45 pregnancies, which were divided into two categories - whether they received preconception consultation or not. Data was collected on patient characteristics, disease duration, medications used, and preconception counselling. Maternal and foetal outcomes were studied.

Results: In this study involving 45 patients, radiographic axial spondylarthritis was the most prevalent type (16 cases), with psoriatic arthritis showing the highest preconception consultation rate (80.0%), with an average of 33.90 years. Lower rates of contraindicated medication were used during pregnancy (0.0%) in counselled patients versus those without counselling (20.0%). Sulfasalazine usage was higher in non-counselled patients (77.8%), while certolizumab pegol use was higher in counselled patients (33.3%). Pregnancy outcomes showed no significant difference in successful pregnancies, but counselled patients experienced significantly fewer postpartum flares (6.4% vs 36.6%). Gestational age at delivery and newborn weight did not significantly differ between groups. Foetal malformation occurred in 2.6% of the population, with no significant difference based on counselling status.

Conclusion: Preconception counselling in women with SpA can increase the likelihood of medication adjustments before pregnancy and decrease the occurrence of flares postpartum. These findings suggest that preconception counselling should be implemented in the management of pregnant women with SpA to improve pregnancy outcomes. Further studies are needed to confirm the effectiveness of preconception counselling and to determine the optimal approach.

Keywords: Reproductive; Spondyloarthropathies (including psoriatic arthritis); Rheumatology; DMARDs; Spondylarthritis.

Introduction

Spondylarthritis (SpA) is a group of chronic inflammatory diseases that mainly affect the axial skeleton and peripheral joints and entheses¹. These conditions encompass several subtypes, divided by predominantly axial SpA (Ankylosing spondylitis, non-radiographic axial spondylarthritis) and peripheral SpA (psoriatic arthritis, Arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondylarthritis)². While these diseases primarily impact the musculoskeletal system, they can also have significant implications for reproductive health, particularly in women of childbearing age.

Pregnancy management in women with SpA requires careful consideration of disease activity and the safety of medications³. Previous research has shown that preconception counselling, a medical consultation that individuals or couples undergo before attempting to conceive a child, and adjustments in medication regimens, can lead to reduced disease flares and improved pregnancy outcomes in women with rheumatoid arthritis⁴. However, the specific impact of preconception counselling on pregnancy outcomes in women with SpA has remained relatively unexplored.

This clinical article presents the findings of a retrospective multicentric study conducted in different regions of Portugal, aiming to investigate the clinical characterization of different spondylarthritis subtypes and the influence of preconception counselling on pregnancy outcomes. By delving into the clinical features of various SpA subtypes and the significance of preconception counselling, we aim to provide valuable insights that can lead to the development of more effective management strategies for optimizing pregnancy outcomes in women with SpA.

Methods

Patient Selection and Design

We designed a retrospective multicentric study that included all patients diagnosed with spondylarthritis made by physician and according to ASAS criteria. Inclusion criteria were pregnant women over 18 years old followed at the Pediatric and Young Adult Rheumatology Clinic at Centro Hospitalar Universitário São João and Centro Hospitalar Tondela-Viseu that had a multidisciplinary appointment with a rheumatologist and an obstetric doctor. Demographic and clinical data were collected. Spondylarthritis was classified using the Assessment in Spondylarthritis international Society (ASAS) criteria.

Data

Data were collected including patient characteristics (age, disease duration, previous pregnancies and previous abortions), preconception (pregnancy on contraindicated medication, biologic disease-modifying anti-rheumatic drugs (bDMARD) started in preconception), medication (Non-steroidal anti-inflammatory drugs (NSAIDs), prednisolone, sulfasalazine, certolizumab pegol), pregnancy outcomes (flare after pregnancy, flare during pregnancy, successful pregnancy), and birth characteristics (gestational age of delivery, newborn weight, foetal malformation, preterm birth and intrauterine growth restriction). Flare was defined as a clinical worsening of symptoms, with increased pain, stiffness and inflammation.

Statistical analysis

Statistical analysis was conducted by using SPSS version 25. Comparisons between groups were evaluated using chi-square (categorical variables), t-test (continuous variables with normal distribution) and Mann-Whitney U test (continuous variables with non-normal distribution). A 2-tailed probability value of $p < 0.05$ was considered statistically significant.

Ethics

The protocol was approved by the Ethics Committee of Centro Hospitalar Universitário de São João and Centro Hospitalar Tondela-Viseu. The study was run in accordance with the principles of the Declaration of Helsinki as amended in Fortaleza (2013).

Results

A total of 45 patients were included in the analysis (Table I), being ankylosing spondylitis the most frequent type (16 cases). Psoriatic arthritis was the group with highest percentage of preconception consultation (8 cases - 80.0%). No cases with juvenile onset were recorded.

Patients had a mean age of 33.90 years and a mean duration of disease of 58.10 months. The patients had an average of 1.20 pregnancies per individual. After dividing the patients into two groups (Table II) – patients with preconception counselling and patients with no preconception counselling – several differences were found.

20.93% (9 cases) of patients had a previous history of abortion in past pregnancies. Preconception counselling did not show a significant association with previous abortion rates (p -value = 0.955).

The use of contraindicated medication during pregnancy was low in patients who received preconception counselling, with no reported cases (0.0%), compared to those without counselling (3 cases - 20.0%), with 2 cases of methotrexate and 1 case of Ustekinumab. This difference was statistically significant (p -value = 0.011).

Regarding specific medications, sulfasalazine usage was higher in patients who did not receive preconception counselling (77.8%) compared to those who received counselling (20.0%), with a statistically significant difference (p -value = 0.002). Conversely, treatment with certolizumab pegol usage was higher in patients who received counselling (33.3%) compared to those without (1 case - 6.7%) (p -value = 0.050). Prednisolone intake did not show a significant difference between the two groups (p -value = 0.612).

When examining pregnancy outcomes, patients who received preconception counselling had a lower rate of successful pregnancies (24 cases - 80.0%) compared to those without counselling (15 cases - 100%), although with no statistical significance (p -value = 0.063).

The occurrence of flares during pregnancy was reported in 33.33% of patients without counselling and in 14.29% of patients with counselling, with no statistically significant difference (p -value = 0.143), having a significantly lower percentage of flares occurring postpartum compared to the non-counselling group (6.4% vs 36.6%, $p=0.031$)

Gestational age at delivery was lower in patients who did not receive preconception counselling (mean of 32.60 weeks) compared to those who received counselling (mean of 38.13 weeks), with no statistical significance (p -value = 0.087). In terms of pregnancy outcomes, 11 C-sections were recorded (3 in women who did not receive preconception), 3 cases of gestational diabetes (all in women who received preconception) and 1 case of pre-eclampsia (women who did not receive preconception). No cases of eclampsia nor gestational hypertension were recorded.

The newborn weight did not show a significant difference between the two groups (p -value = 0.288). The average weight of newborns of patients with preconception counselling was 3243.65 grams, while it was 3227.67 grams in babies born to patients without counselling.

Foetal malformation was a rare occurrence, reported in only 2.6% of total population; there was no significant difference between the two groups (p -value = 0.413). Similarly, there was no statistically significant difference in the rates of preterm birth (p -value = 0.559) or intrauterine growth restriction (p -value = 0.200) between patients with and without preconception counselling.

Discussion

The clinical characterization of different spondylarthritis subtypes is of paramount importance for accurate diagnosis and optimal management. Axial radiographic spondylarthritis was the most prevalent subtype in this study. The percentage of non-radiographic spondylarthritis cases is noteworthy, as it reflects the increasing recognition and diagnosis of this subtype, which may have been previously underdiagnosed⁵.

The variable pregnancy outcomes among different SpA subtypes underscore the need for tailored management strategies. The impact of spondylarthritis on pregnancy outcomes can be influenced by various factors, including disease activity, medication use, and individual patient characteristics⁶. Preconception counselling offers a valuable opportunity for rheumatologists to discuss potential risks and benefits with their patients and create personalized treatment plans to optimize pregnancy outcomes. However, a significant percentage of patients did not undergo preconception counselling in our study, indicating suboptimal monitoring.

The higher percentage of women receiving preconception counselling in the psoriatic arthritis subgroup may indicate increased awareness and proactive management in this patient population. However, it is only of the smallest subgroup, with only 10 cases. Addressing psoriatic arthritis through counselling has previously been linked to better outcomes for both the mother and the baby⁷.

These findings highlight the potential benefits of preconception counselling in reducing disease flares during and after pregnancy and minimizing the usage of contraindicated medications. These results align with previous studies in other rheumatic diseases, such as rheumatoid arthritis, where preconception counselling has been associated with improved pregnancy outcomes⁴.

The impact of spondylarthritis on pregnancy outcomes extends beyond disease activity alone. The use of disease-modifying antirheumatic drugs (DMARDs) during pregnancy poses a complex dilemma⁸. The initiation of biologic DMARDs during preconception counselling highlights the importance of early disease management to achieve better disease control before conception⁹. However, more research is needed to assess the long-term effects of biologic DMARDs on foetal development and the safety of these medications during pregnancy⁹. In this study, there was a statistically significant difference between preconception counselling and no preconception counselling with usage of certolizumab, which may be a key factor in decreasing rates of flare during pregnancy and after pregnancy.

Moreover, patient education and counselling play a crucial role in optimizing pregnancy outcomes in women with SpA. Providing comprehensive information about the disease,

potential risks, and available treatment options empowers patients to make informed decisions about their reproductive health. Counselling can also address concerns about medication adjustments¹⁰. This is highlighted in our study, since a significant higher proportion of patients who did not had preconception counselling had a history of pregnancy with contraindicated medication.

In addition to preconception counselling, ongoing monitoring and disease management during pregnancy are essential for achieving favourable pregnancy outcomes. Regular follow-up visits with rheumatologists and obstetricians allow for close monitoring of disease activity and medication adjustments as needed¹¹. Post-partum flares occurred in 12.19% of patients in our study, which illustrates how crucial it is to monitor this period.

Physical therapy and lifestyle modifications also play a crucial role in the management of SpA during pregnancy. Regular physical activity can help improve joint mobility, reduce pain, and enhance overall well-being. Preconception counselling might be a key moment to promote, helping women maintain an active and healthy lifestyle, and decreasing maternal complications such as gestational diabetes, which occurred in 3 cases.

The findings from the presented studies, together with the broader context of SpA and pregnancy management, underscore the need for continued research in this field. Longitudinal studies that track disease activity and pregnancy outcomes over extended periods can provide valuable insights into the long-term implications of SpA during and after pregnancy.

The limitations of the current studies should also be acknowledged. Retrospective studies inherently carry limitations, including potential selection bias and missing data. Prospective studies that follow patients from preconception through pregnancy and beyond can provide more robust data and better control for potential confounding factors.

Conclusion

In conclusion, spondylarthritis is a group of rheumatologic diseases that can significantly impact pregnancy outcomes in affected women. Ankylosing spondylitis, non-radiographic spondylarthritis, psoriatic arthritis, enteropathic arthritis, and undifferentiated spondylarthritis present unique challenges during pregnancy, necessitating personalized management strategies. Preconception counselling emerges as a crucial intervention to optimize pregnancy outcomes, allowing for the timely adjustment of medications and disease management before conception.

A multidisciplinary approach to managing SpA during pregnancy is essential to achieve favourable outcomes. The involvement of rheumatologists, obstetricians, perinatologists,

physical therapists, nutritionists, and mental health professionals in the care of pregnant women with SpA ensures that all aspects of the patient's health are addressed comprehensively. Collaborative decision-making and regular communication among the healthcare team members are essential to deliver coordinated and patient-centred care.

Accepted manuscript

Tables and Figures

	<u>Ankylosing spondylitis</u>	<u>Non-radiographic axial spondylarthritis</u>	<u>Psoriatic arthritis</u>	<u>Arthritis associated with inflammatory bowel disease</u>	<u>undifferentiated spondylarthritis</u>
Number cases	16/45 (35.6%)	12/45 (26.7%)	10/45 (22.2%)	4/45 (8.9%)	2/45 (4.5%)
Preconception consultation	12/16 (75.0%)	8/12 (75.0%)	8/10 (80.0%)	1/4 (25.0%)	1/2(50.0%)

Table I - SpA patients divided by ASAS classification

	<u>Preconception counselling</u>	<u>No preconception counselling</u>	<u>Total</u>	<u>p-value</u>
<i>Patient Characteristics</i>				
Age (years)	33.43±4.34 (22-41)	33.67±4.81 (27-42)	33.90±4.43 (22-42)	0.990
Months since onset disease	61.93±39.19 (12-168)	42.47±32.95 (5-132)	58.10±41.36 (2-182)	0.177
Previous pregnancies	1.20±1.10 (0-4)	1.73±0.96 (1-4)	1.20±1.16 (0-4)	0.072
Previous history of abortion	6/23 (26.09%)	3/14(21.43%)	9/43(20.93%)	0.955
<i>Preconception</i>				
Pregnancy on contraindicated medication	0/30 (0.00%)	3/15 (20.00%)	3/45 (6.67%)	0.011
bdMARD started in preconception	5/30 (16.67%)	2/15 (13.33%)	7/45 (15.56%)	0.771
<i>Medication</i>				
Prednisolone	6/30 (20.0%)	4/15 (26.67%)	10/45 (22.22%)	0.612
Sulfasalazine	2/30 (6.67%)	7/15 (46.67%)	9/45 (20.0%)	0.002
Certolizumab	10/30 (33.3%)	1/15 (6.67%)	11/45 (24.44%)	0.050
<i>Pregnancy outcomes</i>				
Flare during pregnancy	4/28 (14.29%)	5/15 (33.33%)	9/43 (20.93%)	0.143
Flare after pregnancy	1/26 (3.85%)	4/15 (26.67%)	5/41 (12.19%)	0.031
Successful pregnancy	24/30(80.0%)	15/15(100%)	39/45(86.67%)	0.063
<i>Birth characteristics</i>				
Gestational age	38.13±1.33 (35-40)	38.46±1.13 (36-40)	32.60±13.54 (2-41)	0.087
Newborn Weight (grams)	3243.65±439.45 (2330-4340)	3227.67±428.37 (2520-4200)	2656.20±1310.60 (2-4340)	0.288
Fetal malformation	1/23 (4.35%)	0/15 (0.00%)	1/38 (2.63%)	0.413
Preterm birth	3/24 (12.50%)	1/15 (6.67%)	4/39 (10.26%)	0.559
Intrauterine growth restriction	0/24 (0.00%)	1/15 (6.67%)	1/39 (2.56%)	0.200

Table II – SpA patients divided by having preconception counselling and not having preconception counselling

References

1. Dougados M, Baeten D. Spondyloarthritis. *Lancet*. 2011, 377:2127-2137. [https://doi.org/10.1016/S0140-6736\(11\)60071-8](https://doi.org/10.1016/S0140-6736(11)60071-8)
2. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis*. 2009, 68 Suppl 2:ii1-44. <https://doi.org/10.1136/ard.2008.104018>
3. Mork S, Voss A, Moller S, Bliddal M. Spondyloarthritis and Outcomes in Pregnancy and Labor: A Nationwide Register-Based Cohort Study. *Arthritis Care Res (Hoboken)*. 2021, 73:282-288. <https://doi.org/10.1002/acr.24111>
4. Littlejohn EA. Pregnancy and rheumatoid arthritis. *Best Pract Res Clin Obstet Gynaecol*. 2020, 64:52-58. <https://doi.org/10.1016/j.bpobgyn.2019.09.005>
5. Kameda H, Kobayashi S, Tamura N, et al.. Non-radiographic axial spondyloarthritis. *Mod Rheumatol*. 2021, 31:277-282. <https://doi.org/10.1080/14397595.2020.1830512>
6. Hamroun S, Hamroun A, Bigna JJ, Allado E, Forger F, Molto A. Fertility and pregnancy outcomes in women with spondyloarthritis: a systematic review and meta-analysis. *Rheumatology (Oxford)*. 2022, 61:1314-1327. <https://doi.org/10.1093/rheumatology/keab589>
7. Meissner Y, Rudi T, Fischer-Betz R, Strangfeld A. Pregnancy in women with psoriatic arthritis: A systematic literature review of disease activity and adverse pregnancy outcomes. *Semin Arthritis Rheum*. 2021, 51:530-538. <https://doi.org/10.1016/j.semarthrit.2021.04.003>
8. Levy RA, de Jesus GR, de Jesus NR, Klumb EM. Critical review of the current recommendations for the treatment of systemic inflammatory rheumatic diseases during pregnancy and lactation. *Autoimmun Rev*. 2016, 15:955-963. <https://doi.org/10.1016/j.autrev.2016.07.014>

9. Romanowska-Prochnicka K, Felis-Giemza A, Olesinska M, Wojdasiewicz P, Paradowska-Gorycka A, Szukiewicz D. The Role of TNF-alpha and Anti-TNF-alpha Agents during Preconception, Pregnancy, and Breastfeeding. *Int J Mol Sci.* 2021, 22. <https://doi.org/10.3390/ijms22062922>

10. Dominguez-Solis E, Lima-Serrano M, Lima-Rodriguez JS. Non-pharmacological interventions to reduce anxiety in pregnancy, labour and postpartum: A systematic review. *Midwifery.* 2021, 102:103126. <https://doi.org/10.1016/j.midw.2021.103126>

11. Meissner Y, Fischer-Betz R, Andreoli L, et al. EULAR recommendations for a core data set for pregnancy registries in rheumatology. *Ann Rheum Dis.* 2021, 80:49-56. <https://doi.org/10.1136/annrheumdis-2020-218356>

Accepted manuscript