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## Characterization of the profiles of patients' requiring rheumatological consultation before of assisted reproduction techniques in real-world clinical practice: data from a tertiary rheumatology centre

Marco Tasso<sup>1</sup>, Antonio Schiattarella<sup>2,\*</sup>, Antonio Del Puente<sup>1</sup>, Alfonso Oriente<sup>1</sup>, Rosario Peluso<sup>1</sup>, Giuseppe Coppola<sup>3</sup>, Francesco Caso<sup>1,#</sup>, Luisa Costa<sup>1,#</sup>

<sup>1</sup>Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy.

<sup>2</sup>King's College Hospital NHS Foundation Trust, London, U.K.

<sup>3</sup>Gynecology Unit, Hospital Santa Maria delle Grazie, Pozzuoli, Naples, Italy.

#Co-last authors.

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\*Corresponding author: Antonio Schiattarella, M.D., PhD. Clinical Fellow in Obstetrics and Gynaecology, King's College Hospital NHS Foundation Trust, London, U.K.

Email: aschiattarella@gmail.com.

ORCID: 0000-0003-2994-1093

### ABSTRACT

**Objective.** Infertility is a growing concern, particularly among women with autoimmune diseases, where immune system dysregulation may contribute to both infertility and the development of autoimmune conditions. Assisted reproductive technologies (ART) offer potential solutions for these women, but their impact on autoimmune disease progression remains to be investigated more largely. This study aimed to explore the immunological profiles and previous ART outcomes in women seeking rheumatological consultation prior to ART.

**Materials and Methods.** We analysed data from 80 women attending the Rheumatology Unit of the University of Naples Federico II for pre-ART counselling between January and June 2024.

**Results.** The cohort displayed a high prevalence of autoimmune conditions, including systemic lupus erythematosus (SLE, 23.8%), and significant immunological abnormalities, such as positive antinuclear antibodies (ANA) in 31.3% of patients. Despite a history of previous ART failures and pregnancy losses, most of these patients were on disease-modifying treatments, including biologic DMARDs.

**Conclusions.** Our findings underscore the importance of integrating rheumatological evaluation into pre-ART counselling to optimize reproductive outcomes. A multidisciplinary approach, including collaboration between rheumatologists and fertility specialists, is crucial for mitigating risks and ensuring both maternal and fetal health. Further prospective studies are needed to clarify the effects of autoimmune profiles and treatments on ART success rates and long-term pregnancy outcomes.

### INTRODUCTION

Infertility is defined as the failure to achieve clinical pregnancy after 12 months or more of regular

unprotected intercourse and around 17.5% of the adult population might experience infertility during adult life [1, 2]. Dysregulation of immunity has been documented in women at reproductive

age experiencing infertility, suggesting a potential link between infertility and the subsequent development of autoimmune diseases. Of note, assisted reproductive technology (ART) aimed at aiding fertility and conception can potentially impact the risk of autoimmune disease development [3, 4]. This is related mainly to high oestrogen levels influence T-helper (Th1/Th2) immune balance, which could exacerbate pre-existing autoimmune conditions or trigger immune responses in genetically predisposed individuals. Further, increased regulatory T-cell (Treg) dysfunction could impair immune tolerance, increasing susceptibility to autoimmune diseases [5].

The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have established guidelines to support clinicians in managing these conditions during pregnancy [6,7]. Women with laboratory abnormalities without a diagnosed rheumatic disease represent a challenge. Critical markers such as anti-Ro/SSA, anti-La/SSB, and antiphospholipid antibodies (aPL) must be evaluated during pre-pregnancy assessments to guide management and therapeutic decisions [7,8]. Studies have indicated that antinuclear antibodies (ANA) and anticentromere antibodies may lead to decreased rates of mature oocytes, normal fertilization, cleavage, high-quality embryos, implantation, and pregnancy [9-11]. Despite this evidence, until today, it is critical to refer these patients to rheumatological consultation before of ART techniques.

Our study presents a case series of women who attended our clinic for rheumatological counselling before ART.

## MATERIALS AND METHODS

We analysed data from women attending the Rheumatology Unit of the University of Naples, Federico II, Italy, between January 2024 and June 2024, for counselling before ART. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v. 19.0 (IBM Inc., Armonk, NY). Data are shown as mean  $\pm$  standard deviation (SD), or as number (percentage). This retrospective study utilized anonymized clinical data, and formal ethical committee approval was waived in accordance with Italian regulations. Informed consent was not required due to the retrospective nature of the study and compliance with data protection laws.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

## RESULTS

Our cohort of patient included 80 patients, with a mean age of  $31.3 \pm 6.5$  years. Results were shown in **Table 1**. A total of 5 patients (6.3%) were active smokers. The mean body mass index (BMI) was  $24.7 \pm 4.1$  kg/m<sup>2</sup>. Regarding reproductive history, 32 women had previous abortions, 136 had prior failures of ART procedures. Concerning concomitant treatments, 15 patients (18.8%) were receiving corticosteroid therapy, 26 patients (32.5%) were treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and 14 patients (17.5%) were on biologic DMARDs (bDMARDs). **Table 2** and **Figure 1** outlined the main reasons for rheumatology consultations.

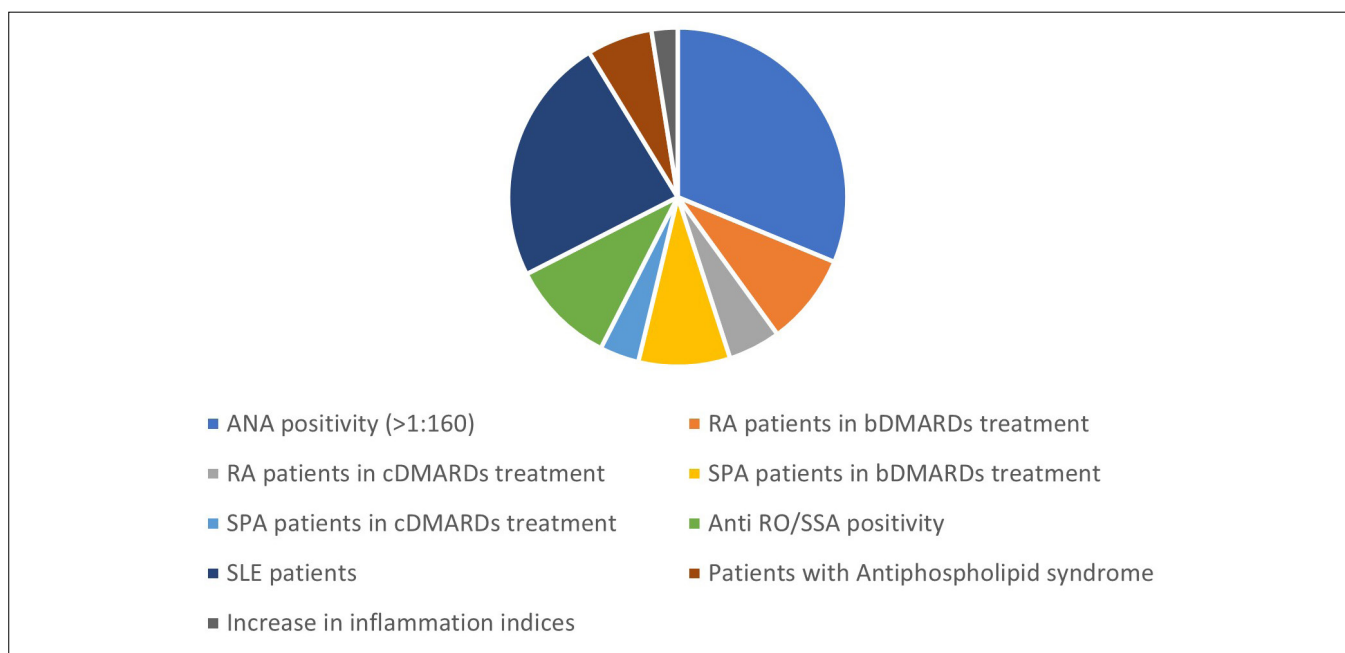
A total of 25 patients (31.3%) demonstrated ANA positivity with titers exceeding 1:160. Regarding treatment regimens, 7 patients with rheumatoid arthritis (RA) (8.8%) were receiving biologic disease-modifying antirheumatic drugs (bDMARDs),

**Table 1.** Demographic information of the 80 subjects.

| Variables                                 |                |
|---|----------------|
| Female, n, %                              | 80, 100%       |
| Age, years, mean $\pm$ SD                 | 31.3 $\pm$ 6.5 |
| Smoking, n, %                             | 5, 6.3%        |
| BMI, mean $\pm$ SD                        | 24.7 $\pm$ 4.1 |
| Number of previous abortions, n           | 32             |
| Number of previous failures "ART", n      | 136            |
| Concomitant corticosteroids therapy, n, % | 15, 18.8%      |
| Concomitant cDMARDs, n, %                 | 26, 32.5%      |
| Concomitant bDMARDs, n, %                 | 14, 17.5%      |

**Table 2.** Reason for rheumatological consultation.

| Variables                                     |           |
|---|-----------|
| ANA positivity (>1:160) n, %                  | 25, 31.3% |
| RA patients in bDMARDs treatment, n, %        | 7, 8.8%   |
| RA patients in cDMARDs treatment, n, %        | 4, 5%     |
| SPA patients in bDMARDs treatment, n, %       | 7, 8.8%   |
| SPA patients in cDMARDs treatment, n, %       | 3, 3.8%   |
| Anti RO/SSA positivity, n, %                  | 8, 10%    |
| SLE patients, n, %                            | 19, 23.8% |
| Patients with Antiphospholipid syndrome, n, % | 5, 6.3%   |
| Increase in inflammation indices, n, %        | 2, 2.5%   |



**Figure 1.** Reason for rheumatological consultation.

while 4 RA patients (5%) were treated with conventional synthetic DMARDs (csDMARDs). Among patients with spondylarthritis (SpA), 7 individuals (8.8%) were undergoing bDMARD therapy, and 3 patients (3.8%) were on csDMARDs. Eight patients (10%) presented anti-Ro/SSA antibody positivity. Additionally, 19 patients (23.8%) were diagnosed with systemic lupus erythematosus (SLE), and 5 patients (6.3%) presented with antiphospholipid syndrome. An increase in inflammatory indices was observed in 2 patients (2.5%).

## DISCUSSION

### Main findings

Our findings showed a substantial proportion of patients with ANA positivity (31.3%), and nearly one-fourth had a diagnosis of SLE (23.8%). The cohort also exhibited a considerable burden of previous ART failures and pregnancy losses, highlighting the complex interplay between rheumatic diseases, immunological status, and reproductive outcomes. Our study underlined the importance of a multidisciplinary approach in the management of women with rheumatic diseases undergoing ART procedures.

### Strengths and limitations

However, our analysis presented several limitations: firstly, the retrospective design of the study inherently restricts the ability to draw causal in-

ferences between disease activity, treatment regimens, and ART outcomes. The relatively limited sample size may restrict the extent to which these findings can be generalized to wider patient populations. The lack of a control group, specifically ART patients without rheumatic diseases, restricts the ability to make direct comparisons. Lastly, data on the actual success rates of ART procedures following counseling and management were not available, preventing a complete evaluation of the impact of pre-ART rheumatologic care on reproductive outcomes. On the other hand, the collection of detailed clinical, immunological, and therapeutic data allows for a comprehensive characterization of the patients' profiles, offering valuable insight into their underlying conditions and treatments. The setting of a tertiary rheumatology centre further contributes to the robustness of the findings, as it reflects real-world clinical practice and enhances the applicability of the results to similar clinical contexts. Additionally, the inclusion of consecutive patients, which helps minimize the risk of selection bias and ensures that the sample accurately represents the population attending the rheumatology unit.

### Interpretation and comparison with other literature

Several studies have investigated the comprehensive characterization of patients requiring rheumatological consultation before undergoing ART. These studies aim to understand the unique challenges and considerations for patients with rheumatic

diseases seeking fertility treatments. They also highlight the necessity for validated protocols for ART in these patient populations to ensure optimal outcomes [7].

The European League Against Rheumatism (EULAR) has developed recommendations focusing on women's health and the management of family planning in patients with SLE and/or antiphospholipid aPL syndrome. These guidelines emphasize the importance of pre-conception counselling, risk stratification based on disease activity, autoantibody profiles, and previous pregnancy outcomes.

Additionally, the Italian Society for Rheumatology has published guidelines on reproductive health, addressing areas such as contraception, ART, pre-conception counselling, and the use of medications before, during, and after pregnancy. These guidelines provide a comprehensive framework for managing patients with rheumatic diseases who are considering ART, ensuring that both maternal and foetal health are prioritized throughout the process [12].

A recent observational multicentre study assessing the efficacy and safety of ART in women with rheumatic diseases showed that ART did not confer additional risks in terms of disease flare-ups or maternal-foetal complications. Moreover, the efficacy of ART was not adversely affected by the presence of maternal rheumatic disease, suggesting that with proper management, patients with these conditions can undergo ART successfully [13]. Furthermore, a study exploring potential barriers to ART utilization emphasized the need for improved patient and clinician education to enhance infertility awareness and ART usage among individuals with rheumatic diseases [14, 15].

Collectively, these studies and guidelines underscore the critical role of comprehensive preconception counselling and tailored management strategies for patients with rheumatic diseases considering ART. They highlight the importance of multidisciplinary collaboration to optimize both rheumatic disease control and reproductive outcomes.

## CONCLUSIONS

Exploration of characterization of patients' profile in this population could offer valuable insights into optimizing reproductive success while minimizing risk of onset and/or flares of rheumatic diseases. In this regard, the establishment of dedicated services

providing a close collaboration between rheumatologists and reproductive medicine specialists represents an useful approach for offering an integrated, patient-centred model of care. Hence, the integration of rheumatological consultation into the pre-ART evaluation process remains key for improving reproductive and maternal outcomes in women with systemic autoimmune diseases or related-serological abnormalities. Future prospective studies with larger cohorts and appropriately matched control groups are advocated to further delineate the influence of specific autoimmune profiles, disease activity levels, and the use of immunosuppressive therapies on ART outcomes. Longitudinal investigations incorporating comprehensive assessments of pregnancy success rates, maternal disease flares, immunological markers, and maternal-fetal outcomes will be essential to refine management strategies for women with rheumatic diseases undergoing assisted reproductive techniques.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors' contribution*

M.T., A.dP., A.O.: Conceptualization. M.T., R.P., G.P.: Data curation. F.C., L.C.: Formal analysis. F.C., L.C.: Methodology. M.T.: Writing – original draft. A.S.: Writing – review & editing.

### *Fundings*

None.

### *Study registration*

N/A.

### *Disclosure of interests*

The authors declare that they have no conflict of interests.

### *Ethical approval*

This retrospective study utilized anonymized clinical data, and formal ethical committee approval was waived in accordance with Italian regulations.

### *Informed consent*

Informed consent was not required due to the retrospective nature of the study and compliance with data protection laws.

### *Data sharing*

N/A.

## REFERENCES

1. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, et al. The International Glossary on Infertility and Fertility Care, 2017. *Fertil Steril*. 2017;108(3):393-406. doi: 10.1016/j.fertnstert.2017.06.005.
2. WHO. 1 in 6 people globally affected by infertility. Available at: <https://www.who.int/news/item/04-04-2023-1-in-6-people-globally-affected-by-infertility>.
3. Scime NV, Velez MP, Choi MY, Ray JG, Boblitz A, Brown HK. Association between infertility and incident onset of systemic autoimmune rheumatic disease after childbirth: a population-based cohort study. *Hum Reprod*. 2025;40(1):157-166. doi: 10.1093/humrep/deae253.
4. Bucci I, Giuliani C, Di Dalmazi G, Formoso G, Napolitano G. Thyroid Autoimmunity in Female Infertility and Assisted Reproductive Technology Outcome. *Front Endocrinol (Lausanne)*. 2022;13:768363. doi: 10.3389/fendo.2022.768363.
5. Desai MK, Brinton RD. Autoimmune Disease in Women: Endocrine Transition and Risk Across the Lifespan. *Front Endocrinol (Lausanne)*. 2019;10:265. doi: 10.3389/fendo.2019.00265.
6. Sammaritano LR, Bermas BL, Chakravarty EE, Chambers C, Clowse M, Locksin M, et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. *Arthritis Care Res (Hoboken)*. 2020;72(4):461-488. doi: 10.1002/acr.24130.
7. Andreoli L, Bertias GK, Agmon-Levin N, Brown S, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. *Ann Rheum Dis*. 2017;76(3):476-485. doi: 10.1136/annrheumdis-2016-209770.
8. Chakravarty EF, Nelson L, Krishnan E. Obstetric hospitalizations in the United States for women with systemic lupus erythematosus and rheumatoid arthritis. *Arthritis Rheum* 2006;54:899-907. doi: 10.1002/art.21663.
9. Bharti B, Lee SJ, Lindsay SP, Wingard DL, Jones KL, Lemus H, et al. Disease severity and pregnancy outcomes in women with rheumatoid arthritis: results from the Organization of Teratology Information Specialists Autoimmune Diseases in Pregnancy Project. *J Rheumatol* 2015;42:1376-82. doi: 10.3899/jrheum.140583.
10. Ying Y, Zhong YP, Zhou CQ, Xu Y, Miao B, Wang Q, et al. Preliminary investigation of the impact of anticentromere antibody on oocyte maturation and embryo cleavage. *Fertil Steril*. 2013;100:1585-1589. doi: 10.1016/j.fertnstert.2013.07.1998.
11. Ying Y, Zhong YP, Zhou CQ, Xu YW, Wang Q, Li J, et al. Antinuclear antibodies predicts a poor IVF-ET outcome: impaired egg and embryo development and reduced pregnancy rate. *Immunol Invest*. 2012;41:458-468. doi: 10.3109/08820139.2012.660266.
12. Fan J, Zhong Y, Chen C. Combined treatment of prednisone and aspirin, starting before ovulation induction, may improve reproductive outcomes in ANA-positive patients. *Am J Reprod Immunol*. 2016;76(5):391-395. doi: 10.1111/aji.12559.
13. Crotti C, Ughi N, Beretta E, Brucato AL, Carrara G, Chimenti MS, et al. The Italian Society for Rheumatology guidelines on reproductive health in patients with rheumatic diseases. *Reumatismo*. 2025;77(1). doi: 10.4081/reumatismo.2025.1752. doi: 10.4081/reumatismo.2025.1752.
14. Reggia R, Andreoli L, Sebbar H, Canti V, Ceccarelli F, Favaro M, et al. An observational multicentre study on the efficacy and safety of assisted reproductive technologies in women with rheumatic diseases. *Rheumatol Adv Pract*. 2019;3(1):rkz005. doi: 10.1093/rap/rkz005.
15. Peninger E, Leavitt M, Edens C, Venkatachalam S. Fertility and the Use of Assisted Reproductive Technologies: Perceptions, Thoughts and Experiences of Men and Women with Rheumatic Disease [abstract]. *Arthritis Rheumatol*. 2022;74(suppl 9). Available at: <https://acrabstracts.org/abstract/fertility-and-the-use-of-assisted-reproductive-technologies-perceptions-thoughts-and-experiences-of-men-and-women-with-rheumatic-disease/>.