

Critical Commentary on the Recently Published Evaluation and Treatment of Infertility in a Clinical Case of a Subfertile Couple in the *New England Journal of Medicine (NEJM)*

Murcia Lora José María*

Department of Restorative Reproductive Medicine, Clinical Consulting G&E, 26002, Logroño, La Rioja, Spain

***Corresponding Author:** Murcia Lora José María, Department of Restorative Reproductive Medicine (RRM), Clinical Consulting G&E, 26002, Logroño, La Rioja, Spain.

Received: May 16, 2025; **Published:** June 09, 2025

Abstract

The *New England Journal of Medicine (NEJM)* has recently published a clinical case of an unsuccessful infertile couple with a desire to become pregnant after one year of having intercourse two to three times a week without contraception [1]. This article presents this short anamnesis to study the clinical pathways to resolve the infertility problem of the couple who would like to have three children. This is a very rare situation that does not represent a reason for consulting in the regular clinical practice to be an example in the solving of fertility problems with assisted reproductive techniques (ART), as well as to be published as a reference clinical case in the evaluation and treatment of infertility in the *NEJM*.

Keywords: Fertile Window; NaProTechnology; Fertility Awareness; Subfertility; Restorative Reproductive Medicine (RRM)

Introduction

It is acknowledged that evaluating functional disorders of subfertility can be a challenging process, often requiring a significant investment of time and medical resources, which in some cases ends with good results. This case seems to tend to justify at first instance *in vitro* fertilization (IVF) or intrauterine insemination (IUI) [1]. Ovulation assessment is discussed very little in the article without considering other fertility approaches such as the Creighton Fertility Care System (CrMS) model, The Billings Ovulation Method (MOB), Natural Procreation Technology (NaProTechnology), Restorative Reproductive Medicine (RRM) or multidisciplinary approaches to the fertile window [2-7].

Comment

In order to conduct a comprehensive and accurate fertility evaluation, it is essential to address several clinical points in an infertile couple. There is no medical finding of pathology, and the woman is 36 years old with menstrual cycles. The anamnesis, as always, should be guided by the reason for consultation, and there is apparently some interest in retinoids, lithium and methotrexate, as well as androgenic steroid use in males in the United States (US), which is unusual in a fertility study at a quick overview in general. This is not a reference for infertility problems in the general world population, which creates an analysis apparently biased from the outset by the reference population to which the authors refer [1].

Citation: Murcia Lora José María. "Critical Commentary on the Recently Published Evaluation and Treatment of Infertility in a Clinical Case of a Subfertile Couple in the *New England Journal of Medicine (NEJM)*". *EC Gynaecology* 14.6 (2025): 01-03.

The evaluation of functional cycle disorders is a process that is generally considered to require a comprehensive approach, as well as a significant investment of time. This approach is costly, but in some cases it is effective. There are alternatives such as natural fertility, which has recently been reviewed by an expert committee of the journal *Sterility and Fertility* [2]. This study [1] proposes IVF in the first place when it is also known that the delay in time to attempt pregnancy (TTP) is probably an important factor, and not necessarily the age of the patient justifies IVF in this case according to the article [1]. TTP improves with fertile window detection [7]. Only with this methodology the patient probably could have had a chance of pregnancy. Ovulation assessment is very poor if based on Luteinizing Hormone (LH) alone, without taking into account other strategies in the study of the fertile window as can be seen in recent publications such as the iNEST study, the OPTUM study, Hilgers' NaProTechnology protocols, Boyle's charts, and their step-by-step assessment of ovulation quality, RRM approach, the MOB or a multidisciplinary assessment of the fertile window [3-7,10].

Within the recommendations for routine testing, semen testing is referred to as one of the first, however, as a first step in the clinical approach to the infertile couple it is important to consider a fertility study. Regarding the types of treatment proposed in the article [1], it can be pointed out that IVF, IUI and gamete donation techniques are contemplated. At present, it is well known that there are alternatives to ART that can help to solve the different problems that arise in infertility [3-5,7].

Treatment of varicocele leads to pregnancy in some cases, however the alternative in the clinical case presented is IUI without any other treatment and study opportunity for the male [1]. The ovarian reserve test is placed as a very important factor, when in general the infertility problem should be focused on the assessment of the quality of ovulation.

The authors [1] give a lot of importance to premature/primary ovarian insufficiency (POI). In the article there are no symptoms to suspecting POI. A multicentric study has been published recommending caution in the assessment of Anti-Müllerian-Hormone (AMH) values, especially in extreme groups [8]. As also recommended by Steiner [9], the altered AMH value alone does not indicate that it is not possible to obtain a mature follicle. Within the guidelines of the European Society of Human Reproduction and Embryology (ESHRE), routine ovarian reserve testing in early pregnancy is not recommended in cases with regular menstrual cycles [2].

Regarding hydrosalpinx, the authors themselves say that depending on the case, it is not necessarily necessary to operate on hydrosalpinx, as was previously known [11]. Small fibroids do not necessarily affect fertility, as Somigliana says in his article [12]. Further, the approach to the uterine septum is complex to evaluate and it is not clear whether surgery is always necessary; in this regard, the article is conservative [13].

Pregnancies can be achieved with treatment of endometriosis, whether medical, surgical or both [14], unlike what is suggested in the article that proposes IVF as treatment [1]. At the same time, it is prudent to take into account the cervical factor and not to bypass it, as is often the case in ART protocols. In the case of the article [1], IUI is considered a basic option associated with conventional follicular stimulation protocols without considering other options.

The conclusion could perhaps be improved by a more balanced focus, including the potential challenges of infertility of unknown origin and exploring a range of options for achieving pregnancy, beyond the initial intention of three children through IVF. It might also be beneficial to consider the side effects associated with ART [15].

Conclusion, Summary and Practical Applications

In general, the evaluation of organic and functional cycle disorders in subfertile couples requires a comprehensive, lengthy and cost-effective approach, which in some cases has yielded good results with other low-cost alternative therapies without negative side effects.

Bibliography

1. Santoro N and Polotsky AJ. "Infertility evaluation and treatment". *New England Journal of Medicine* 392.11 (2025): 1111-1119.
2. Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Reproductive Endocrinology and Infertility. "Optimizing natural fertility: a committee opinion". *Fertility and Sterility* 117.1 (2022): 53-63.
3. Stanford JB., *et al.* "International Natural Procreative Technology Evaluation and Surveillance of Treatment for Subfertility (iNEST): enrollment and methods". *Human Reproduction Open* 2022.3 (2022): hoac033.
4. Kuroda K., *et al.* "Novel approaches to the management of recurrent pregnancy loss: The OPTIMUM (Optimization of Thyroid function, Thrombophilia, Immunity, and Uterine Milieu) treatment strategy". *Reproductive Medicine and Biology* 20.4 (2021): 524-536.
5. Marshall M., *et al.* "Stratification of fertility potential according to cervical mucus symptoms: achieving pregnancy in fertile and infertile couples". *Human Fertility (Camb)* 24.5 (2021): 353-359.
6. Murcia Lora JM. "Multidisciplinary Fertile Window Assessment for Ovulation Diagnosis". *Academia Letters* (2021): 3980.
7. Hilgers Thomas W. "The Medical & Surgical Practice of NaProTechnology". 1st edition. Pope Paul VI Institute Press: Omaha, Nebraska, USA (2004).
8. Huang Y., *et al.* "Using anti-Müllerian hormone to predict premature ovarian insufficiency: a retrospective cross-sectional study". *Frontiers in Endocrinology (Lausanne)* 15 (2024): 1454802.
9. Steiner AZ., *et al.* "Association between biomarkers of ovarian reserve and infertility among older women of reproductive age". *Journal of the American Medical Association* 318.14 (2017): 1367-1376.
10. Boyle PC., *et al.* "Healthy singleton pregnancies from restorative reproductive medicine (RRM) after failed IVF". *Frontiers in Medicine (Lausanne)* 5 (2018): 210.
11. Murcia Lora JM. "Assessment & diagnostic test to check free pathways for sperm swimming in the genital tract". *Academia Letters* (2021): 3309.
12. Somigliana E., *et al.* "Fibroids and natural fertility: a systematic review and meta-analysis". *Reproductive BioMedicine Online* 43.1 (2021): 100-110.
13. Blanco-Breindel MF., *et al.* "Septate Uterus". In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing (2025).
14. Yeung P., *et al.* "The long-term rate of repeat surgery after optimal excision surgery of endometriosis at a single tertiary referral center". Preprints (2024): 2024091485.
15. Alcázar Zambrano JL. "Riesgos para la salud en los niños concebidos mediante Técnicas de Reproducción Asistida". First edition. Early Institute, A.C. earlyinstitute.org. (2018).

Volume 14 Issue 6 June 2025

©All rights reserved by Murcia Lora José María.