ESHRE 41st Annual Meeting

P-457: Increased prevalence of specific KIR phenotypes in a population of unexplained infertility with implantation failure and recurrent pregnancy loss: A retrospective study

Zavala-Garcia, Abraham[1], Izquierdo-Urdinola, Hector[1], Serrano-Palomo, Laura[2], Horcajadas, Jose A.[2], Padure, Sergiu[4]

1. Assisted Reproduction Unit, Tambre Advanced Reproductive Medicine, Alicante, Spain
2. Tambre Foundation, Madrid, Spain
3. SINAE, Research Department, Seville, Spain
4. Reproductive Immnulogy Unit, Tambre Advanced Reproductive Medicine, Madrid , Spain

Introduction

Killer immunoglobulin-like receptors (KIR) and **human leukocyte antigen (HLA)** interactions are **key modulators of immune responses for implantation**. Previous studies suggest that specific KIR phenotypes, particularly KIR-BX and KIR-AA (lacking 2DS1, 2DS5, and 3DS1), could be associated with adverse reproductive outcomes, including recurrent implantation failure (RIF) and recurrent pregnancy loss (RPL). HLA molecules, especially HLA-C, interact with KIRs to influence natural killer cell function at the maternal-fetal interface.

Methodology

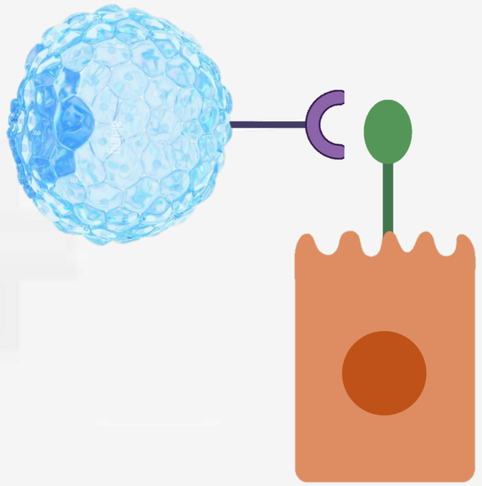
This retrospective observational study reviewed patient records from January 2022 to December 2024 at a fertility clinic's reproductive immunology unit. We analyzed 293 patients with unexplained infertility presenting as RIF or RPL. Data regarding KIR and HLA genotypes were collected along with immunological parameters. The study aimed to evaluate the frequency and distribution of individual KIR and HLA phenotypes as well as their combinations, with a specific focus on known pathologic KIR types.

Study Question:

In a population of patients with unexplained infertility with RPL or RIF, **do certain KIR-HLA phenotypes or their combinations have an increased prevalence?**

Summary Answer:

KIR phenotypes Bx and AA were found overrepresented in this RIF/RPL population.



This study included **293 patients with unexplained infertility with either RPL or RIF detected at our fertility clinic** and referred to our reproductive immunology unit.

Results

We determined the frequencies of KIR and HLA phenotypes. **KIR BA (37.20%, p=0.372) emerged as the most common phenotype**, followed by KIR-AA, BX, and BB. Among **HLA phenotypes, C1/C2 (45.73%) was slightly more frequent than other phenotypes**. The **most frequently observed KIR–HLA pairing was KIR-AA–HLA-C1C2, even though KIR-AA was not the most prevalent phenotype overall.**

Although KIR phenotypes Bx and AA, previously linked to adverse reproductive outcomes, were common individually, neither reached a majority threshold. However, **when combined as a 'pathologic KIR' group, these types accounted for 55.3% (n=162) of the cohort**. A one-sample proportions test using chi-square statistic yielded a **p-value=0.039**, indicating a statistically significant overrepresentation of pathologic KIR.

Conclusions

Despite emerging evidence linking certain KIR and HLA combinations to infertility, results remain inconsistent and further investigation is needed to clarify their role in unexplained infertility cases as demonstrated previously.

These findings contribute to a growing body of evidence on the immunogenetic factors influencing reproductive outcomes. Although further validation is necessary, the **overrepresentation of pathologic KIR phenotypes** may guide future research and therapeutic strategies in managing unexplained implantation failure and recurrent pregnancy loss, and ultimately enhance targeted personalized treatment outcomes.