Session title: Implantation and early pregnancy
Session type: Poster viewing
Presentation number: P-440

★ Abstract title:

HLA-C haplotypes distribution among gametes donors in our population

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Study question:

HLA-C haplotypes distribution among gametes donors in Caucasian population

Summary answer:

Among oocyte donors, 37.5% have an HLA-C1C1 haplotype, and very similar among sperm donors 32%.

What is known already:

Increased risk of recurrent miscarriage (RM), preeclampsia and fetal growth restriction has been described in mothers KIR AA when the fetus has more HLA-C2 genes than the mother with a higher incidence in oocyte donation pregnancies compared to spontaneous conception or IVF pregnancies. In oocyte donation, the oocyte HLA-C behaves as the paternal HLA-C increasing the number of non-self-antigens presented to the mother´s uterine immune cells. This KIR-HLA-C combination is still not considered nowadays in the process of donor selection. KIR AA patients have lower live birth rates (LBR) after double embryo transfer (DET) oocyte-donation, especially with HLA-C2 partner.

Study design, size, duration:

Between April 2015 and October 2017, we performed a prospective study that included 783 gametes donors matched for couples with recurrent miscarriage or recurrent implantation failure of unknown etiology. We performed HLA-C typing for 683 oocytes donors and for 100 sperm donors.

Participants/materials, setting, methods:

All the donors were selected from IVIRMA Clinics, and showed a normal karyotype, negative serology and fulfilled our standards for gamete donation. We did genetic typing for HLA-C after obtaining signed informed consent. HLA-C haplotype distribution among oocytes and sperm donors in our Caucasian Spanish population was analyzed.

Main results and the role of chance:

In our cohort of 683 oocytes donors, we observed a 37.5% HLA-C1C1 haplotype (N= 256), 47.7% HLA-C1C2 and 14.8% HLA-C2C2. Among the sperm donor cohort, HLA-C haplotype distribution was 32% for HLA-C1C1, 50% for HLA-C1C2 and 18% for HLA-C2C2.

Knowing the HLA-C distribution in our gametes donors might be helpful as LBR is lower when women KIR AA received a C2 donor, especially when they have a HLA-C2 partner and the embryo has more HLA-C2 antigens than the mother. This first study, observed a 32-37% of HLA-C1C1 frequency among gametes donors in our population. Those KIR-HLA-C mismatched couples affected by recurrent miscarriage or recurrent implantation failure may benefit from this approach.

Limitations, reasons for caution:

The study's objective was to describe the HLA-C distribution among our donors cohort and the frequency of what we may consider the "best" haplotype, HLA-C1C1. This is the first study observing the HLA-C distribution among gametes donors and represent useful data.

Wider implications of the findings:

It's believed that completing a normal pregnancy is possible only for KIR AA mothers who carry a baby with a least one non-–self HLAC1. During oocyte donation, the KIR-HLA-C mismatch increases compared to own oocytes. Therefore, selecting HLA-C1 among donors could be more efficient and safer, for specific couples.