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# FEMALE 21-OH CONGENITAL ADRENAL HYPERPLASIA CARRIER STATUS IS NOT ASSOCIATED WITH SUBOPTIMAL IMPLANTATION RATES AFTER A SINGLE EUPLOID EMBRYO TRANSFER

Carlos Hernandez-Nieto, MD[1], Teresa A. Cacchione, MS, CGC[1], Deborah Cassis-Bendeck, MD[1], Joseph A. Lee, BA[1], Beth McAvey, MD[2], Tanmoy Mukherjee, MD[1], Benjamin Sandler, MD[1] and Alan B Copperman, MD[1]

1. Reproductive Medicine Associates of New York, New York, NY
2. Icahn School of Medicine at Mount Sinai, New York, NY

**OBJECTIVE:** Female carriers of 21-OH Deficient Congenital Adrenal Hyperplasia (21-OH CAH) might experience hormonal disturbances in androgen biosynthesis.[1,2] Given the critical role played by steroid hormones in reproductive function and endometrial receptivity, it is plausible that individuals affected by these steroidogenic disorders might face potential fertility challenges. Limited research has been published about the relationship between patients who are heterozygous carriers for this disorder, infertility, and implantation potential after IVF. Our study aims to evaluate the reproductive potential of 21-OH CAH carriers who undergo single euploid embryo transfer (SET).

**MATERIALS AND METHODS:**
Patients who underwent SET on a synthetic preparation cycle from 2018 to 2021. PGT-A with *NGS* was performed for all cases. All couples underwent preconception expanded carrier screening. Patients were segregated into 2 groups based on female *CYP21A12* carrier status (Heterozygote carriers; vs Non-carriers*)*. Patients with biallelic *CYP21A2* mutations were excluded. Baseline characteristics, hormonal profiles, and pregnancy outcomes were compared between cohorts. Comparative statistics and an adsuted multivariate analysis with a GEE was performed. A sample size of 100 patients per cohort was calculated to ensure an 80% power to detect a difference of 15% on implantation rates (α=0.05)

**RESULTS:**
3,337 SET cycles were included in the analysis. 187 21-OH CAH carriers (5.6% prevalence) were compared against 3,150 non-carriers. No differences were found in age at ET, oocyte age, BMI, baseline estradiol, progesterone, FSH, LH, AMH among groups, also no differences were found on serum estradiol and serum progesterone levels the day of progesterone start between cohorts. A significant difference was found in mean endometrial thickness at ET (9.7 ±2.2 vs 9.4 ±2.0,p=0.01) and 17-OH progesterone levels (91.8 ±612 vs 415 ±521,p=0.02) between cohorts. Furthermore, embryo quality at ET, implantation rate, ongoing pregnancy, clinical pregnancy and clinical pregnancy loss rates were comparable between cohorts. In a multivariate analysis after adjusting for age, BMI, AMH, day of embryo biopsy, embryo quality and endometrial thickness, no association was found between being a 21-OH CAH carrier and lower odds of implantation (OR 0.8 CI95% 0.5-1.2), clinical pregnancy (OR 0.7; 0.5-1.09), ongoing pregnancy rate (0.7; 0.5-1.06), or higher odds of clinical pregnancy loss (OR 1.12; 0.6-1.8)

**CONCLUSIONS:**
It had been suggested that 21-OH CAH carriers might experience some degree of disruption in 21-hydroxylase enzymatic activity, raising concern about the potential impact on endometrial receptivity and IVF outcomes. However, despite a mild hyper-androgenic profile, 21-OH CAH carriers present similar implantation rates and IVF outcomes after a SET compared to non-carriers.

**IMPACT STATEMENT:**
This study is first to show patients who are heterozygous carriers for 21-OH CAH do not appear to experience suboptimal implantation rates and/or pregnancy outcomes compared to non-carriers after IVF with a single euploid embryo transfer.

**REFERENCES:**

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