DIFFERENCES IN IVF OUTCOMES BETWEEN PATIENTS WITH BRCA1 AND BRCA2 MUTATION

Authors: Ng A (1), Tarrash M (2), Ilg D (2), Peyser A (2), Goldman R (2), Singer T (2)

Affiliations: (1) Dept. Of Ob/Gyn, Zucker School of Medicine at North Shore/LIJ, Manhasset, NY, USA; and (2) Northwell Health Fertility, Zucker School of Medicine at North Shore/LIJ, Manhasset, NY, USA

Background

BRCA1 and BRCA2 are tumor suppressor genes that are integral to the DNA repair process and mutations in these genes are found in roughly 1 in 300 to 1 in 800 people, most commonly in Ashkenazi Jews [1]. Monoallelic pathogenic variants in these genes are known to significantly increase the risk of epithelial ovarian and breast cancer, among other cancers [2]. Furthermore, patients with BRCA mutations exhibit lower levels of AMH and earlier menopause [3]. As a result, patients with BRCA mutations often undergo IVF/ICSI/PGT-M even in the absence of infertility. Whether a difference in outcomes exists between BRCA1 and BRCA2 patients is understudied.

Objective

We aim to compare IVF/ICSI, PGT-A, and PGT-M outcomes between patients with BRCA1 or BRCA2 mutations at a single academic tertiary center.

Materials and Methods

This is a retrospective cohort study of patients 18-43 years old who underwent genetic counseling for personal, partner, or family history of BRCA1 and/or 2 mutation between July 2017 and October 2024. Among the 36 unique patients identified to be carriers for BRCA1 or BRCA2, 25 patients who elected to undergo fertility treatment were eligible for inclusion. Cycle characteristics (age at retrieval, AMH, FSH, stimulation days, peak estradiol level [E2 Max], and total gonadotropins), as well as IVF/ICSI/PGT-A/PGT-M outcomes (number of oocytes retrieved, number of MII, number of 2PN, D5, D6, D7, number of biopsied blastocysts, euploid, euploid ratio, and BRCA affected embryos) were collected. Cycles with male factor <5 million and incomplete/cancelled cycles were excluded, leaving 23 unique patients and 39 total cycles for analysis. Patients were then stratified by BRCA1 or BRCA2 mutation and a two-tailed T-test assuming equal variances was performed for each of the parameters.

Result(s)

Thirty-nine cycles were included in the study, of which 51% (20/39) were of BRCA1 positive patients and 49% (19/39) were of BRCA2 positive patients. When comparing the 2 groups, patients were found to have similar cycle characteristics including age, AMH, FSH, stimulation days, peak E2 level, and total gonadotropin use. BRCA2 patients were found to have a higher number of oocytes retrieved ($p=0.05$), MII's ($p=0.04$), and 2PN's ($p=0.03$). In addition, BRCA2 patients reached D5 blastocyst phase more often than BRCA1 patients ($p=0.02$). Within the IVF/ICSI/PGT cohort, 17% (6/34) of cycles had PGT-A performed, while 82% (28/34) had both PGT-A and PGT-M. There were no differences between euploid ratio or BRCA1/2 mutation in the embryos (Table 1).

Table 1: Cycle characteristics, IVF, PGT-A, and PGT-M outcomes between BRCA1 and BRCA2 patients

	BRCA1 (n=20)	BRCA2 (n=19)	p value
Age at Retrieval	33.9±4.0	32.4±4.2	0.26
AMH	2.1±1.3	3.1±2.1	0.08
FSH	6.4±2.6	6.9±3.2	0.67
Stim Days	10.0±1.8	10.2±1.6	0.63
E2 Max	1470.0±1666.2	1896.5±2177.4	0.50
Total Gonadotropins	3806.9±1436.3	3536.1±1531.4	0.58
# Oocytes Retrieved	12.4±7.7	19.3±12.9	***0.05**
# MII	9.7±6.1	15.3±9.8	***0.04**
# 2PN	7.3±5.4	12.2±7.2	***0.03**
D5	1.4±2.1	3.8±3.8	***0.02**
D6	3.0±2.7	3.7±2.9	0.47
D7	0.2±0.5	0.0±0.0	0.26
Biopsied Blastocysts	4.5±3.8	6.9±3.0	0.06
Euploid	2.3±2.2	3.2±2.3	0.25
Euploid Ratio	0.5±0.3	0.4±0.2	0.37
BRCA 1/2 Affected	2.5±2.1	2.6±2.4	0.88

Conclusion

In our study, patients affected by the BRCA2 gene mutation were found to have a higher number of oocytes retrieved, MII's, and 2PN's when compared to those with BRCA1 mutation. In addition, BRCA2 patients reached D5 blastocyst phase more often than those with BRCA1 mutation despite similar cycle characteristics. These findings may be helpful when counseling BRCA patients undergoing IVF/ICSI/PGT-A/PGT-M for fertility preservation and family planning. Further studies are warranted to investigate the impact of BRCA1 and BRCA2 on IVF outcomes.

Financial Support
None

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